TRENDS OVER TIME IN THE PREVALENCE OF CLOSTRIDIUM DIFFICILE WITHIN A LARGE COMMUNITY HOSPITAL SETTING: 1997-2017

by

Benjamin James Hampton

BA, Edinboro University of Pennsylvania, 2009

BS, University of Pittsburgh at Greensburg, 2015

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This essay was submitted

by

Benjamin James Hampton

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and approved by

Essay Advisor:
Evelyn O Talbott, DrPH, MPH _____
Professor
Departmental of Epidemiology
Graduate School of Public Health
University of Pittsburgh

Essay Readers:

Joanne Russell, MPPM _____
Assistant Professor, Behavioral and Community Health Sciences
Director, Center for Global Health
Assistant Dean, Global Health Programs
Graduate School of Public Health
University of Pittsburgh

John Love, MD, PhD _____
Infectious Disease Specialist
Butler Health System
Butler Memorial Hospital
Butler, Pennsylvania

Evelyn O Talbot, DrPH, MPH

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ABSTRACT

Background/Objective: The epidemiology of *Clostridium difficile* has changed dramatically in recent years, marked by increases in incidence and severity of disease. This growing public health problem affects both community and healthcare acquired cases, leading to increased mortality due to the emergence of hypervirulent strains and antibiotic resistance. The overall objective of this study is to determine trends in *C. diff* over time in a large community hospital over the twenty years from 1997-2017.

Methods: A retrospective chart review of patients at a 321-bed acute care community hospital in Western Pennsylvania from mid-1997 to the present was conducted. The server database was supplied by Meditech. ICD-9 codes of 8.45, indicating *Clostridium difficile* Infection (CDI or *C. diff* infection), either upon admission or during hospitalization were obtained in addition to age, race, gender, length of stay, disposition status, zip code of residence, admission status (nursing home, residence) and payer status for each patient. *C. diff* infection status was determined by enzyme immunoassay until Dec 2011 and then was switched to current PCR method.

Results: A total of 72, 884 patient encounters were tested for *C.diff* between 1985 and 1997 and followed forward from 1997-2017 to determine subsequent *C. diff* testing. Of this cohort, Butler County encounters were selected and those under 18 (3,598) as well as those who were observation encounters (1,072) were excluded, leaving a cohort of 54,789 Butler County Encounters. GIS

mapping of *C. diff* prevalence rates indicated an increasing trend of *C. diff* over the 20-year period. Overall, there was a higher proportion of outpatients with both a history of *C. diff* and a subsequent positive *C. diff* test among encounters over age 65 and among nursing home residents. Analysis confirmed that the relative risk of a patient testing positive for *C. diff* is higher if there was a previous positive test - especially among those over 65 and nursing home residents. Logistic regression analysis indicated that a prior history of *C. diff* as the single biggest predictor of a subsequent positive test, controlling for other factors.

Conclusion: There is increasing evidence of *C. diff* prevalence in Butler County over the 20-year period, probably reflecting a large nursing home population and an overall aging population. Prevention efforts should include increased educational efforts aimed at handwashing and containment and notification of each *C. diff* case upon diagnosis.

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LIST OF ACRONYMS

BMH	Butler Memorial Hospital
CA-CDI	Community-acquired *Clostridium difficile* infection
CDI	*Clostridium difficile* infection
GIS	Geographic information system
HA-CDI	Healthcare-acquired *Clostridium difficile* infection
LOS	Length of stay
MDC	Major Diagnostic Category
NH	Nursing home
PPI	Proton pump inhibitor
RR	Relative risk
SHEA	Society for Healthcare Epidemiology of America
TCD	Toxigenic *Clostridium difficile*

PREFACE

I would like to thank Dr. Thomas McGill and Dr. John Love for inviting me to Butler Memorial Hospital's Infectious Disease Department for my internship, for being my preceptors and mentors, and for their kind patience throughout this process. Next, I would like to thank Dr. Nancy Glynn for her help securing my internship, for being available when I needed assistance, and for her willingness to help me achieve my goals as a graduate student. I would also like to thank Dr. Evelyn Talbott for her guidance as my graduate and essay advisor and for the time she has invested in my success. Finally, I would like to thank Joanne Russell for her unwavering support in all my endeavors at Pitt Public Health.

1.0 INTRODUCTION

The purpose of this essay is fourfold. The first goal is to present the descriptive epidemiology of the population at risk for *Clostridium difficile* in Butler County, Pennsylvania. The second goal is to present the trends of *Clostridium difficile* prevalence in the United States and compare them to the trends over a 20-year period in a large community hospital setting in Western Pennsylvania. Third, while many studies have investigated the incidence, prevalence, and risk factors for CDI, none known have attempted to use geographic information systems (GIS) to analyze trends over time at a zip code level. This essay will present information regarding *C. diff* prevalence rates in Butler County, Pennsylvania using GIS to help visualize and analyze patterns and trends in CDI prevalence in this community. The final goal is to confer the subsequent risk of testing positive for *C. diff* based on a prior history of *C. diff.*

1.1 CLOSTRIDIUM DIFFICILE

1.1.1 History

The first account of a disease resembling *Clostridium difficile* appeared in the *Bulletin of the Johns Hopkins Hospital*.[1] On July 28, 1892, Dr. John Miller Turpin Finney, the first President of the American College of Surgeons, described *C. diff* in a 22-year-old female who developed

mild diarrhea after gastric surgery.[1,2] Five days later she died from the condition, which had progressed to frequent bloody stools.[1] It wasn't until 1978 that Bartlett and colleagues first identified *C. diff* as a gram-positive, anaerobic, toxic spore-forming bacteria that caused antibiotic-associated diarrhea and pseudomembranous colitis.[3,4]

1.1.2 Clostridium difficile in the United States

C. diff is an important infectious disease in the field of public health and clinical practice due to its increasing incidence and severity in previously-low risk populations and to the growing incidence of community-acquired and asymptomatic *C. diff* over the past 10-15 years.[5,6,7] This increase in population vulnerability and incidence has led to more frequent complications from *C. diff* infection (CDI) as well as increased healthcare costs and mortality.[6] *Clostridium difficile* infection has surpassed rates of methicillin-resistant Staphylococcus *aureus* in some areas of the United States to become the most common healthcare-associated infection.[6] The reasons for this increase include 1. an aging population with more comorbidities, 2. increased antibiotic use and resistance, and 3. the emergence of hypervirulent strains of *Clostridium difficile*.[8]

In fact, the number of people discharged with CDI in the US has nearly doubled, increasing from 31/100,000 population in 1996 to 61/100,000 in 2003.[6,7] Additionally, between 2000-2008 the number of hospital stays with any CDI discharge diagnose increased 2.5-fold from 139,000 to 349,000 while discharges with a primary diagnosis of CDI increased 3.5-fold from 32,800 to 114,000 in the same period.[6] In 2009 community-acquired CDI estimates in the US were between 8 and 12/100,000 population, occurring in younger, healthy populations that lack traditional CDI risk factors. The cause of CDI in the community is unknown but possible sources include food or zoonotic pathogens.[7] In 2011, CDC active surveillance data from 10 Emerging Infections Program

sites in 34 counties covering 11.2 million people, identified 15,461 cases; 65.8% of these infections were healthcare-associated (defined as community-onset associated with a healthcare facility, hospital-onset, or nursing home-onset) while only 24.2% had hospital-onset.[9] The study estimated that the incidence of community-acquired *Clostridium difficile* infection (CA-CDI) in the United States after accounting for age, sex, and race was 51.9/100,000 population while the estimated incidence of healthcare-associated *Clostridium difficile* infection (HA-CDI) was 95.3/100,000 population. Overall, there were an estimated 453,000 incident infections and 29,000 CDI-related deaths in 2011. These estimates were higher among females (RR: 1.26), whites (RR: 1.72), and individuals 65 and older (RR: 8.65). In addition, the estimated 345,000 cases that occurred outside of hospitals, 46.2% of which were estimated to be community-acquired, highlight the need to direct prevention efforts toward the community setting.[9]

1.2 CLINICAL PRACTICE GUIDELINES

1.2.1 Diagnosis and Treatment of *Clostridium difficile* Infection

According to the 2010 Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA), healthcare providers are advised to test for *C. diff* on unformed stools only; testing of asymptomatic patients is not recommended as it is "not clinically useful".[10] When treating CDI, the antibiotic used should be based on the local epidemiology and strains of the bacteria while the antibiotic that initiated the infection should be discontinued immediately. The first line of treatment for initial mild to moderate CDI is 500 mg of metronidazole three times a day for 10 to 14 days. For initial severe infection, 125 mg of

vancomycin taken four times a day for 10 to 14 days is recommended. Severe and complicated cases of CDI call for vancomycin delivered by oral (500 mg four times daily) or rectal (500 mg in 100 ml saline per rectum every six hours as retention enema) route with or without 500 mg of intravenous metronidazole every eight hours. If unresolved, colectomy is recommended for severely ill patients.[10]

1.2.2 Infection Control for *Clostridium difficile*

Regarding infection control, the use of gloves and gowns when entering the room of a patient with CDI is recommended; proper hand hygiene is of utmost importance.[10] It is advised that CDI patients have a private room, but double-occupancy is acceptable if the infected patient has a dedicated restroom facility. Testing of asymptomatic carriers is not currently recommended. For sanitation purposes, guidelines recommend using chlorine-based or sporicidal agents in areas of frequent CDI. It is important for providers to practice antibiotic stewardship by minimizing how often and how long antibiotics are prescribed, reducing the number of different antibiotics prescribed, and restricting the use of cephalosporins and clindamycin as they are associated with increased risk of CDI.[7,10]

1.3 HOSPITAL-ACQUIRED CLOSTRIDIUM DIFFICILE

In 2011, the CDC estimated that the incidence of HA-CDI was 95.3/100,000 population.[9] Definitions for HA-CDI vary in the literature; several studies define HA-CDI as symptoms occurring more than 48 hours after admission[11,12] or less than four weeks after discharge.[11] Another

study by Kuntz et al. defined HA-CDI as a secondary CDI diagnosis during hospitalization or a primary diagnosis of CDI on admission with no hospital discharge within 12 weeks or diagnosis as outpatient with hospital discharge history in four weeks before diagnosis.[13] While the definition differs, all studies found that the incidence of HA-CDI has increased over the last 20 years. Khanna and colleagues showed a 19.3-fold increase of incident HA-CDI between 1991 – 2005 based on all potential CDI cases in Olmsted County, Minnesota. Incidence increased from 2/100,000 person-years in 1991-1993 to 40.2/100,000 person-years in 2003-2005.[11]

On the other hand, a population-based, retrospective, nested case-control study of CDI cases based on healthcare claims in a database at the University of Iowa College of Public Health found HA-CDI incidence of 12.41/100,000 person-years based on 2004-2007 data.[13] Globally, the incidence of HA-CDI is consistently significantly higher in adults 65 and older.[9,11,12] A prospective study in southeast Scotland found the overall incidence of HA-CDI to be 44.7/100,000 person-years among those 18 and older with a significantly proportion of cases having been prescribed antibiotics in the eight weeks prior to diagnosis. Among those 65 and older, the incidence was 164.1/100,000 person-years with those over 75 more likely to have HA-CDI. Researchers also discovered that 13.3% of HA-CDI cases were co-infected with norovirus, which means that the incidence of HA-CDI could be over-reported; the role of co-infections has not been widely studied. Overall, studies agree that incidence of HA-CDI is significantly associated with advanced age, antibiotic use, and the use of proton pump inhibitors (PPIs) and H2 antagonists. [11-17]

1.4 COMMUNITY-ACQUIRED CLOSTRIDIUM DIFFICILE

The definition of CA-CDI varies as much as the definition for HA-CDI. Many studies agree that to be classified as CA-CDI, symptoms must occur in admitted patients within 48 hours and with no hospital discharge of CDI.[9,11,13,18] However, CA-CDI is also defined as the first hospital admission with a primary ICD-9 code of 008.45, as CDI onset with no healthcare contact in the 12 weeks prior to diagnosis, and as a positive *C. diff* toxin or molecular assay from a patient who did not have a positive test in the previous eight weeks.[19,12,20] Therefore, rates of CA-CDI can vary substantially.

In Olmsted County Minnesota, 41% of CDI cases between 1991 and 2005 were community acquired with an age and sex-adjusted incidence of 9.6/100,000 person-years (25.2/100,000 person-years overall).[11] Over the 14-year study period, incidence of CA-CDI increased 5.3-fold from 2.8/100,000 person-years in 1991 – 1993 to 14.9/100,000 person-years in 2003-2005. Patients with CA-CDI were also less likely to have severe CDI than those with HA-CDI.[11] In contrast to HA-CDI, patients with CA-CDI are younger, more likely to be female, less likely to have comorbidities, less likely to have previous antibiotic exposure, and are less likely to be on PPIs or H2 blockers.[11]

One case-control study also showed that CA-CDI occurs in about 40% of CDI cases; however, results showed that patients were more likely to have prior hospitalizations and to have taken antibiotics or gastric acid suppressors than control subjects.[13] This important difference between HA-CDI and CA-CDI highlights CDI in populations who were previously thought to be low-risk such as young adults and children who do not have traditional CDI risk factors.[6,11,13] Among a random sample of Medicare beneficiaries aged 65 and older from 2009 - 2011, 38% were determined to have CA-CDI with an overall CA-CD incidence in this population of 0.18%.[19] This

high proportion of community-acquired cases highlights the emerging importance of the community as a source of CDI. Consistent with the literature on community-acquired *C. diff*, these patients were more likely to be female; however, within the 65 and older population, patients with CA-CDI were more likely to be in their 80s. Similar to other studies of CA-CDI, while antibiotics play a significant role in HA-CDI, almost half of CA-CDI cases were not exposed to antibiotics, which indicates that this exposure may not be a significant risk for CA-CDI. The study concluded that CA-CDI affects generally healthy elderly Americans in this population.[19] Among patients with confirmed CA-CDI in a population-based surveillance study for CDI in 10 states in 2009, Chitnis et al. reported that 82% of patients had recent outpatient healthcare exposure.[20] This suggests that healthcare exposure could be a significant source of *Clostridium difficile* in the community.

1.5 ASYMPTOMATIC CLOSTRIDIUM DIFFICILE

Asymptomatic CDI is of concern in the field of public health as its role in the spread of community-acquired and healthcare-acquired is still unclear. A study at Barnes-Jewish hospital in Missouri investigated prevalence and risk factors for asymptomatic *C. diff* carriage by comparing isolates from asymptomatic carriers to those with CDI.[21] The prevalence of asymptomatic toxigenic *C. diff* on admission was 15% (an increase from previous studies); however, no clear risk factors were discovered. While the strains isolated from carriers were similar to those found in patients with CDI, the distribution was different. Unlike previous studies, there was no association between colonization and antibiotic or healthcare exposure; 90% of TCD carriers and 85.3% of uncolonized patients had at least one inpatient and/or outpatient healthcare exposure within 90 days prior to admission, indicating nosocomial infection at the healthcare source. The

researchers suggested a higher incidence of community-acquired infection than previously thought as a reason for this discrepancy. The high percentage of asymptomatic carriers indicates that this population may be a significant source of new *C. diff* infections as these individuals shed the bacteria into their environment.[21] These results call for a review of clinical practice guidelines as testing asymptomatic patients is not currently recommended.[10] Another study at St. Mary's Hospital in Minnesota found a 9.7% asymptomatic TCD colonization rate among eligible patients.[14] Researchers recommend active surveillance and contact precautions for asymptomatic carriers due to the risk as an important route of *C. diff* transmission; however, the study acknowledged the challenge of receiving a sample in ample time after admission as a limitation to implementing active surveillance measures.[14]

1.6 ECONOMIC BURDEN OF CLOSTRIDIUM DIFFICILE

In 2008, the estimated acute direct costs of CDI were $4.8 billion US dollars (USD).[6] When indirect costs, management of the disease, and recurrent infections are taken into consideration, this is estimate is likely to be higher. Epidemiological studies on HA-CDI often do not account for the economic burden of CDI on recently-discharged patients, outpatients, and those who are released to long-term care facilities.[6] Among Medicare beneficiaries, one in five are readmitted for recurrent CDI within one month; this high recurrence rate places an increasing economic burden on members, insurers, and facilities.[19] In addition, the higher rate of colectomy in this population contributes to the high cost of the disease.[19] As the leading cause of infectious diarrhea among hospitalized patients, understanding the costs has direct implications on policy and treatment decisions while reducing the cost to hospitals, third-party carriers, and society is

increasingly important to overall rising healthcare costs. In a computer-simulated model, McGlone and colleagues estimated the burden of HA-CDI in US hospitals.[22] Investigators modeled 1,000 adults 65 and older 1,000 times for a total of one million outcomes. The cost per case of HA-CDI ranged from $8,932 to $16,464 in 2010 USD; a six-day hospital LOS attributed to CDI cost an estimated $9,197; severe cases with a 10-day LOS cost an estimated $10,187. Third party costs for one case began at a baseline of $10,123 and the societal cost of one case with a six-day LOS began at a baseline cost of $14,726. In summary, the model suggested that the annual economic burden of CDI on the US was over $496 million from the hospital perspective, over $547 million from a third-party perspective, and over $796 million from a societal perspective.[22] As these estimates are several years old, limited to patients 65 and older, and do not take CA-CDI into account, the actual economic burden of CDI in the United States is likely to be significantly higher, highlighting the importance of surveillance, prevention, control, and antibiotic stewardship in reducing the cost of the disease.

1.7 PUBLIC HEALTH SIGNIFICANCE

The epidemiology of *Clostridium difficile* infection is changing; community acquired infections are occurring more often in younger populations and other populations not previously considered at risk. Gaps in the knowledge surrounding the sources of *C. diff* in the community, the risk factors for CA-CDI, and the role of asymptomatic carriers is of increasing public health significance that requires further research. Incidence of *Clostridium difficile* infection has increased over the last 20 years due to emerging severe strains, antibiotic resistance, and lack of surveillance; these factors have led to increased difficulty surrounding treatment and prevention.

It is important to pursue research that contributes to the knowledge of the etiology and spread of this increasingly threatening infectious disease. Additionally, with an aging population that is at higher risk for CDI, increasing incidence will undoubtedly lead to continued rising healthcare costs from CDI.

2.0 OBJECTIVES

The goal of this analysis is to determine the trends in *C. diff* over time in a large community hospital over the twenty years from 1997-2017.

- The first objective is to describe the change in trends in prevalence of *Clostridium difficile* infection within a large community hospital in Western Pennsylvania over time.
- The second objective is to map and investigate the change in trends in hospital prevalence of *Clostridium difficile* infection by zip code.
- The third objective is to estimate subsequent risk of testing positive for *C. diff* given a prior *C. diff* test result
- The fourth objective is to compare findings to trends described in the literature.

3.0 RESEARCH METHODS AND ANALYSIS PLAN

Patient data for this study were collected from Butler Memorial Hospital (BMH), a 321-bed acute care community hospital in Western Pennsylvania. This facility is the primary medical/ laboratory in the region, making it an ideal location to study county *C. diff* rates and trends. A 2010 report on Pittsburgh migration illustrates that Butler County has a stable population. From 2000 to 2010, net migration in Butler fluctuated by only a few hundred people as compared to neighboring counties such as Allegheny County, which fluctuated by over 1,000 individuals from year to year.[23] At BMH, electronic medical records (EMR) are stored on a 2008 Meditech SQL Server R2 and, until 2011, the hospital used enzyme immunoassay to test for *C. diff* at which time a molecular testing method was put into place. In 1985, BMH began keeping EMR; the data used in this study include in and outpatient EMR from 1985 to present divided into two phases. The first phase, or capture phase, (1985-1997) is based on all in- and outpatients who were ever tested for *C. diff*. The second phase is the follow-up phase. In this phase, patients from the capture phase are followed forward from 1997-March 2017 to determine additional *C. diff* test results in this period. The de-identified data was obtained with permission from the Butler Health System Data Privacy and Security Committee on July 30, 2016 (**Appendix**).

A total of 72,884 patient encounters (34,322 unique individuals) represent the history of *C. diff* testing in this date range as shown in **Figure 1**, Research Methodology Flowchart. These patients were then followed forward from 1997-March 2017. The following variables were also collected and utilized in analysis: De-identified patient number, a unique ID given to every patient to enable identification of multiple hospital visits and multiple *C. diff* tests; age; race; gender; postal code; date of visit; primary diagnosis code (ICD-9 and ICD-10); major diagnostic category;

whether *C. diff* was present at admission, as indicated by a positive *C. diff* test result within two days of admission where day of admission is day zero; *C. diff* test result, the result of a *C. diff* test on an unformed stool; whether the patient was inpatient or outpatient; disposition status; nursing home status, whether or not a patient originated from a nursing home; and history of *C. diff*, whether the patient had a history of *C. diff*, based on any *C. diff* test result from 1985 – 2017.

Non-Butler residents were excluded from this cohort of 72,884 patient encounters, leaving 59,424 Butler County encounters (26,847 individuals) (based on zip code) who were selected for analysis. This population was chosen due to its stability. Further excluded from analysis were 3,598 encounters (2,523 individuals) under the age of 18 as well as 1,072 observation encounters (605 individuals) – 35 of these observation encounters (26 individuals) were under 18. The final study population was 54,789 Butler County encounters (23,745 individuals). All data were de-identified and analyzed using SPSS Statistics 24. Mapping was completed using ArcMap 10.4.1.

The primary research questions included the following:

1. What are the trends over the study period of 1997 – 2017 regarding rates of *Clostridium difficile* at Butler Memorial Hospital and how do these trends compare to national rates over the last 20 years? Do these trends differ by age?
2. Are there any spatial trends (by zip code) by age and gender regarding *C. diff* infection rates in Butler County, Pennsylvania?
3. What are the risk factors for testing positive for *Clostridium difficile* among those tested?
4. Is there a difference in *C. diff* history between inpatients versus outpatients?
5. Does having a positive *C. diff* history increase the risk of a subsequent positive *C. diff* test?

This study is a cross sectional investigation of trends over time and *C. diff* status as of March 2017. In addition, this study has a retrospective cohort component; the data were collected by going back to 1985 EMR and querying any patient who had ever been tested for *C. diff* until 1997. These patients were then followed from 1997-2017 to determine if they were tested for *C. diff* in this period and, if so, whether the result was positive. Butler County's 38 postal codes were the primary units of analysis as well as 2010 census information for the denominator variable. The following analyses were conducted:

1. A descriptive analysis of the inpatient and outpatient population by age, race, and gender as well as by *C. diff* testing prior to baseline (*C. diff* history) and *C. diff* test result overall during the follow up period by major diagnostic category.
2. A comparison of the overall age and gender adjusted and age and gender specific rates of *C. diff* prevalence rates over four time periods (1997 – 2001, 2002 – 2006, 2007 – 2011, and 2012 – 2017). A linear test for trends was carried out to determine if the rates were significantly different over time for both inpatient and outpatient visits using individual visits as well as patient encounters.
3. Using ArcMap 10.4.1, *C. diff* prevalence rates by zip code for the four time periods were considered to the extent permitted by the data.
4. Logistic regression was utilized to determine risk factors for a positive *C. diff* test result based on prior history.

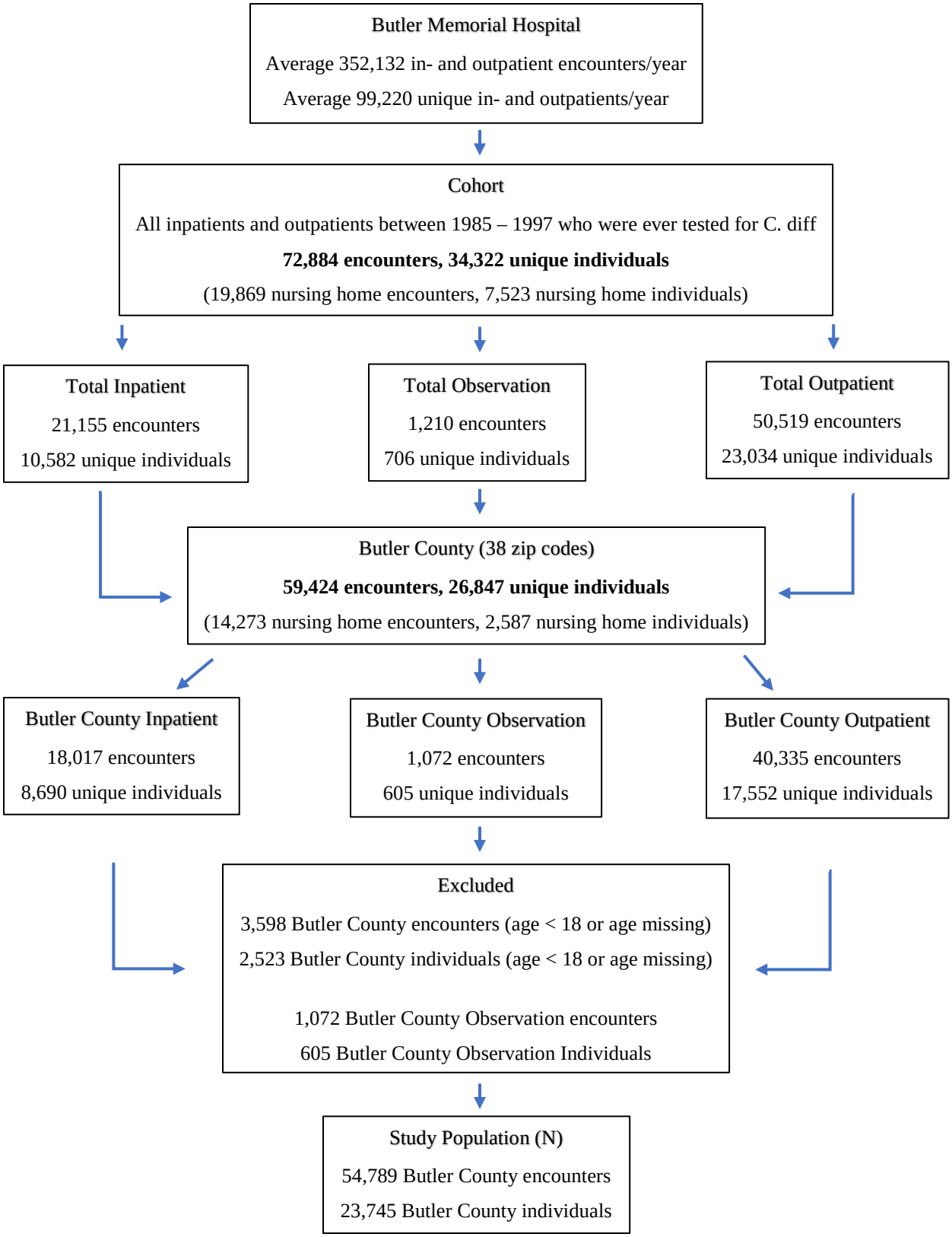


Figure 1. Research Methodology Flowchart

4.0 RESULTS AND ANALYSIS

4.1 TOTAL POPULATION CHARACTERISTICS

During the follow-up period (February 1997-March 31, 2017), there were 54,789 inpatient and outpatient encounters with Butler County residents who were previously tested for *C. diff* in the capture phase (1985-1997). These encounters consisted of 33,140 females (60.5%) and 21,649 males (39.5%) over 18 years of age. These individuals were 89% White (53.2% female and 35.9% male) and had a mean age of 70.6 and 68.0, respectively (**Tables 1** and **3**). Of this population, 14,158 (25.8%) were residents of a nursing home with a mean age of 80.0. Among nursing home residents, 9,541 (17.4% of the total study population) were females with a mean age of 81.3 and 4,617 (8.4% of the total study population) were males with a mean age of 77.3. Not unexpectedly, a much older average age was noted among nursing home resident encounters at BMH (**Table 2**).

Table 1. Gender and Age Characteristics of Study Population by Race: Butler Memorial Hospital Patient Encounters over Age 18 (Butler County Residents Only) with a Prior *Clostridium difficile* Test History between 1985 and 1997 (N = 54,789)

		N	% of Total Cohort	$\bar{x}$ (age)	SD
Female					
	White	29,155	53.2	69.1	17.3
	Black or African American	139	0.25	64.2	15.6
	Asian	22	0.04	66.0	14.8
	Hispanic	17	0.03	46.7	15.4
	Other	39	0.07	64.7	15.5
	Unknown or Missing	3,768	6.9	82.3	11.1
	Total	**33,140**	**60.5**	**70.6**	**17.3**
Male					
	White	19,658	35.9	67.1	16.0
	Black or African American	109	0.19	66.8	16.0
	Asian	33	0.06	66.3	21.4
	Hispanic	30	0.05	54.5	14.9
	Other	34	0.06	62.5	15.3
	Unknown or Missing	1,785	3.3	78.9	12.5
	Total	**21,649**	**39.6**	**68.0**	**16.0**
Total	**Males and Females**	**54,789**	**100.0**	**69.6**	**16.8**

Table 2. Gender and Age Characteristics of Nursing Home Population (N = 14,158) within Total Cohort (N = 54,789): Butler Memorial Hospital Nursing Home Encounters over Age 18 (Butler County Residents Only) with a Prior *Clostridium difficile* Test History between 1985 and 1997

	N	% of Total Cohort	$\bar{x}$ (age)	SD
Female	9,541	17.4	81.3	9.9
Male	4,617	8.4	77.3	11.3
Total Nursing Home	**14,158**	**25.8**	**80.0**	**10.5**
Total Non-Nursing Home	**40,631**	**74.2**	**65.9**	**17.1**
Total Cohort	**54,789**	**100.0**	**69.6**	**16.8**

Most of the total study population (36,839, or 67.2%) was over 65 years old while 17,950 (32.8%) were between ages 18-64 (**Table 3**). Among both age groups, there were more women than men. In the 18-64 age group, there were 10,127 women (56.4%) and 7,823 men (43.6%) and in the 65 and over age group, there were 23,013 women (62.5%) and 13,826 men (37.5%).

Table 3. Gender and Age Characteristics of Butler Memorial Hospital Encounters Ages 18-64 and 65+ within Total Cohort (N = 54,789): Gender by Age Group among Butler County Residents with a Prior *Clostridium difficile* Test History between 1985 and 1997

	18-64			65+			Total		
	N	% 18-64	$\bar{x}$ age	N	% 65+	$\bar{x}$ age	N	% Total	$\bar{x}$ age
Female	10,127	56.4	49.0	23,013	62.5	80.1	33,140	60.5	70.6
Male	7,823	43.6	50.56	13,826	37.5	77.9	21,649	39.5	68.0
Total	**17,950**	**100.0**	**49.7**	**36,839**	**100.0**	**79.3**	**54,789**	**100.0**	**69.6**

Tables 4 and **5** show the age distribution of the population at entry into the cohort among men versus women and among inpatients versus outpatients. Women were the majority in all age groups (**Figure 2**) and were, on average, older with a mean age of 70.6 versus 68.0 for men (**Table 4**). There was also a higher percentage of outpatients versus inpatients for each age group and a higher percentage of outpatients overall (67.3% vs. 32.7%) as shown in **Figure 3**; however, the average inpatient was older at 70.7 versus 69.0 for outpatients (**Table 5**).

Table 4. Butler Memorial Hospital Patient Encounters over Age 18 (In and Outpatient) with a Prior History of Testing for *Clostridium difficile* between 1985-1997: Age Distribution by Gender (at entry into the cohort) Among the Total Study Population (N = 54,789)

	$\bar{x}$ = 70.6 (SD = 17.3) **Female**		$\bar{x}$ = 68.0 (SD = 16.0) **Male**		$\bar{x}$ = 69.6 (SD = 16.8) **Total**		
Age, years	N	%	N	%	N	%	$\bar{x}$ age
<30	1,134	62.5	679	37.5	1,813	100.0	24.2
31-44	2,063	61.3	1,302	38.7	3,365	100.0	38.4
45-54	2,490	54.1	2,109	45.9	4,599	100.0	50.1
55-64	4,440	54.3	3,733	45.7	8,173	100.0	59.8
65-79	10,605	57.2	7,932	42.8	18,537	100.0	72.6
80+	12,408	67.8	5,894	32.2	18,302	100.0	86.0
Total	33,140	60.5	21,649	39.5	54,789	100.0	69.6

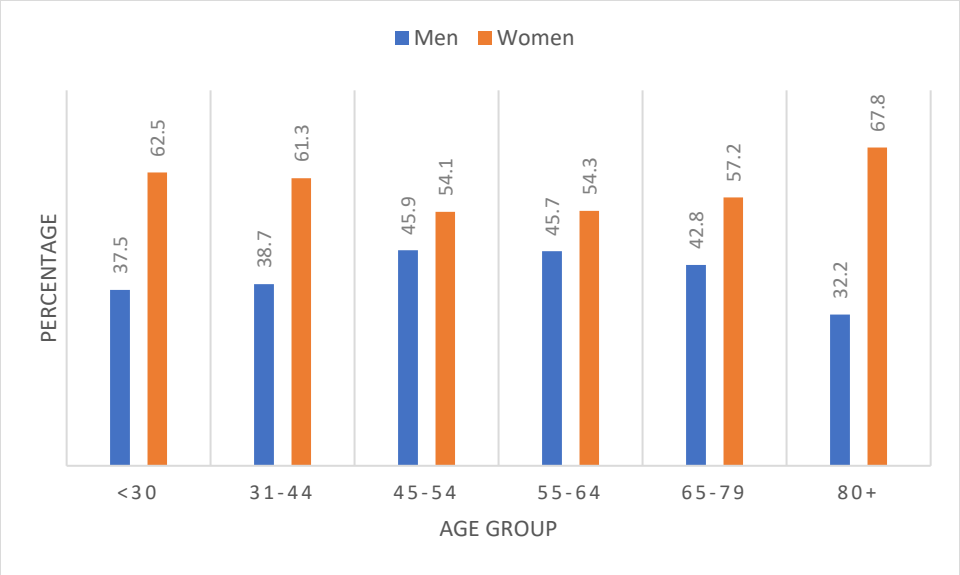


Figure 2. Butler Memorial Hospital Patient Encounters over Age 18 (In and Outpatient) with a Prior History of Testing for *Clostridium difficile* between 1985-1997: Percent Men and Women by Age Group (at entry into the cohort) Among the Total Study Population (N = 54,789)

Table 5. Butler Memorial Hospital Patient Encounters over Age 18 (In and Outpatient) with a Prior History of Testing for *Clostridium difficile* between 1985-1997: Age Distribution by Patient Type (Inpatient and Outpatient) by Age Group (at entry into the cohort)

	$\bar{x}$ = 70.7 (SD = 15.3) **Inpatient**		$\bar{x}$ = 69.0 (SD = 17.5) **Outpatient**		$\bar{x}$ = 69.6 (SD = 16.8) **Total**		
Age, years	N	%	N	%	N	%	$\bar{x}$ age
<30	336	18.5	1,477	81.5	1,813	100.0	24.2
31-44	924	27.5	2,441	72.5	3,365	100.0	38.4
45-54	1,437	31.2	3,162	68.8	4,599	100.0	50.1
55-64	2,589	31.7	5,584	68.3	8,173	100.0	59.8
65-79	6,700	36.1	11,837	63.9	18,537	100.0	72.6
80+	5,951	32.5	12,351	67.5	18,302	100.0	86.0
Total	17,937	32.7	36,852	67.3	54,789	100.0	69.6

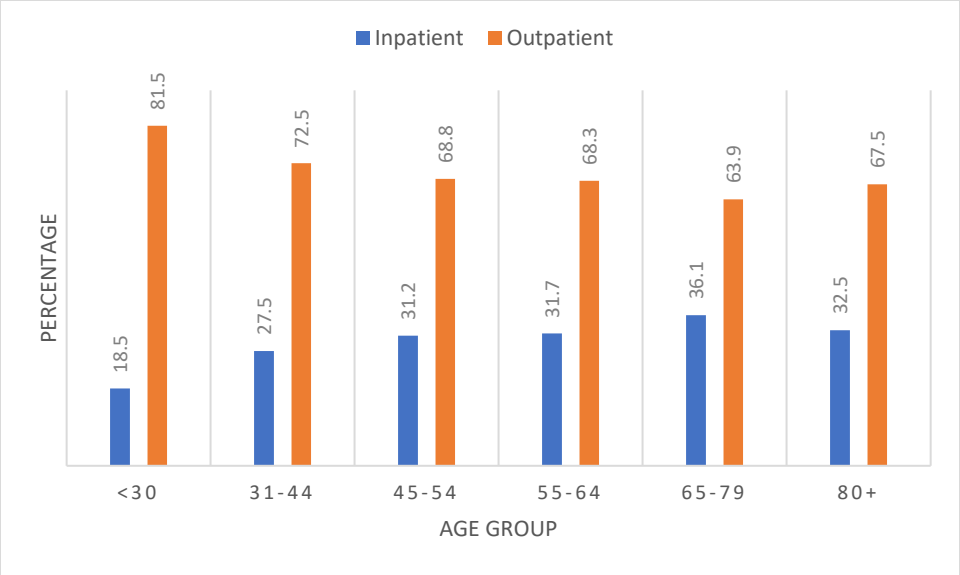


Figure 3. Butler Memorial Hospital Patient Encounters over Age 18 (In and Outpatient) with a Prior History of Testing for *Clostridium difficile* between 1985-1997: Percent Inpatient and Outpatient by Age Group (at entry into the cohort) Among the Total Study Population (N = 54,789)

4.2 HISTORY OF CLOSTRIDIUM DIFFICILE

As shown in **Table 6**, among inpatients, 16,202 (90.3%) had no history of *C. diff* and 1,735 (9.7%) had a history of *C. diff* while among outpatients, there were 32,607 (88.5%) and 4,245 (11.5%) with no history and history of *C. diff*, respectively. Interestingly, a positive history of *C. diff* among outpatients was almost three percent higher than among inpatients. A Chi-Square Test of Independence shows a significant association between patient type (inpatient vs. outpatient) and prior history of *C. diff* ($p = .000$) as there was a higher percentage of inpatients with no history of *C. diff* than expected and lower percentage of inpatients with a history of *C. diff* than expected. Among outpatients there was a lower percentage without a history of *C. diff* than expected and a higher-than-expected percentage of outpatients with a history of *C. diff*.

Table 6. Butler Memorial Hospital Patient Encounters over Age 18 by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$ (age)	SD
Inpatient	1,735	9.7	16,202	90.3	17,937	100.0	70.7	15.3
Outpatient	4,245	11.5	32,607	88.5	36,852	100.0	69.0	17.5
Total	5,980	10.9	48,809	89.1	54,789	100.0	69.6	16.8

$\chi^{(1)} = 42.297$, p = .000

Among inpatients ages 18-64, 4,753 (89.9%) had no history of *C. diff* while 533 (10.1%) had a history of *C. diff* (**Table 7**). There were 11,563 (91.3%) outpatients with no history of *C. diff* and 1,101 (8.7%) with a positive history. Compared to the total study population (**Table 6**), there was a higher percentage of inpatients with a history *C. diff* among those 18-64 (10.1% vs. 9.7%) and a smaller percentage with a positive history among outpatients (8.7% vs. 11.5%). A Chi-Square test (p = .003) indicates a slightly higher-than-expected percentage of inpatients with a history of *C. diff* than outpatients.

Table 7. Butler Memorial Hospital Patient Encounters Ages 18-64 by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$ (age)	SD
Inpatient	533	10.1	4,753	89.9	5,286	100	51.3	10.8
Outpatient	1,101	8.7	11,563	91.3	12,664	100	49.0	12.5
Total	1,634	9.1	16,316	90.9	17,950	100	49.7	12.1

$\chi^{(1)} = 8.699$, p = .003

Both outpatients 65+ and those originating from a nursing home (**Table 8** and **9**) had a slightly higher percentage of outpatients with a history of *C. diff* than inpatients (p = .000) at 13.0% and 18.1%, respectively. This high percentage of outpatient encounters with a positive history of *C. diff* suggests that much of the burden of *C. diff* on Butler Memorial Hospital is due to patients

who get *C. diff* in a nursing home rather than contracting the infection at BMH itself. **Table 9** also shows the advanced mean age of outpatient nursing home encounters (80.9), a well-known risk factor for *C. diff* infection.

Table 8. Butler Memorial Hospital Patient Encounters Ages 65+ by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$ (age)	SD
Inpatient	1,202	9.5	11,449	90.5	12,651	100.0	78.8	7.6
Outpatient	3,144	13.0	21,044	87.0	24,188	100.0	79.5	8.2
Total	4,346	11.8	32,493	88.2	36,839	100.0	79.3	8.0

$\chi^{(1)} = 97.619$, p = .000

Table 9. Butler Memorial Hospital Nursing Home Resident Patient Encounters by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$ (age)	SD
Inpatient	451	10.4	3,873	89.6	4,324	100.0	78.1	10.6
Outpatient	1,781	18.1	8,053	81.9	9,834	100.0	80.9	10.4
Total	2,232	15.8	11,926	84.2	14,158	100.0	80.0	10.5

$\chi^{(1)} = 133.415$, p = .000

Table 10 shows the history of *C. diff* among patient encounters in the follow-up period based on two age groups: 18-64 and 65+. These are the ages of the patients at entry into the cohort. Among those aged 18-64, 16,316 (90.9%) had no history of *C. diff* and 1,634 (9.1%) had a history of *C. diff*. Among those 65+, 32,493 (88.2%) had no history of *C. diff* and 4,346 (11.8%) had a history of *C. diff*. Not unexpectedly, there were a higher number of patient encounters with a previous history of *C. diff* among the older cohort (p = .000).

Table 10. Butler Memorial Hospital Patient Encounters (In and Outpatient) over Age 18 by Age Group (18-64 and 65+) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$ (age)	SD
18-64	1,634	9.1	16,316	90.9	17,950	100.0	49.7	12.1
65+	4,346	11.8	32,493	88.2	36,839	100.0	79.3	8.0
Total	5,980	10.9	48,809	89.1	54,789	100.0	69.6	16.8

$\chi^{(1)} = 90.101$, p = .000

Among female encounters, 29,412 (88.8%) had no history of *C. diff* while 3,728 (11.2%) had a history of *C. diff*. On the other hand, 19,397 (89.6%) of male encounters had no history of *C. diff* and 2,252 (10.4%) had a history of *C. diff* (**Table 11**). There was a slight increase in the number of women with a *C. diff* history compared to males (11.2% versus 10.4%) (p = .002).

Table 11. Butler Memorial Hospital Patient Encounters (In and Outpatient) over Age 18 by Gender and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	3,728	11.2	29,412	88.8	33,140	100.0	70.6	17.3
Male	2,252	10.4	19,397	89.6	21,649	100.0	68.1	16.0
Total	5,980	10.9	48,809	89.1	54,789	100.0	69.6	16.8

$\chi^{(1)} = 9.660$, p = .002

Table 12 shows that among female encounters aged 18-64, 9,160 (90.5%) had no history of *C. diff* while 967 (9.5%) had a history of *C. diff*. Among male encounters of the same age group, there were 7,156 (91.5%) with no history of *C. diff* and 667 (8.5%) with a history of *C. diff*. (p = .018).

Table 12. Butler Memorial Hospital Patient Encounters (In and Outpatient) Ages 18-64 by Gender and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	967	9.5	9,160	90.5	10,127	100.0	49.0	12.4
Male	667	8.5	7,156	91.5	7,823	100.0	50.6	11.6
Total	1,634	9.1	16,316	90.9	17,950	100.0	49.7	12.1

$\chi^{(1)} = 5.578$, p = .018

While **Tables 11** and **12** showed a higher-than-expected number of female encounters with a history of *C. diff*, **Table 13** indicates *C. diff* history among female and male encounters aged 65+ is very similar. Among female encounters, 20,252 (88.0%) had no history of *C. diff* while 12,241 (88.5%) male encounters had no history of *C. diff*. There were 2,761 (12.0%) female encounters with a history of *C. diff* and 1,585 (11.5%) male encounters with a history of *C. diff*. All counts are as expected (p = .124).

Table 13. Butler Memorial Hospital Patient Encounters (In and Outpatient) Ages 65+ by Gender and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	2,761	12.0	20,252	88.0	23,013	100.0	80.1	8.1
Male	1,585	11.5	12,241	88.5	13,826	100.0	77.9	7.6
Total	4,346	11.8	32,493	88.2	36,839	100.0	79.3	8.0

$\chi^{(1)} = 2.364$, p = .124

Like females and males ages 65+, among patients who originated from a nursing home, there was no significant difference between the number of females and males (Chi-Square p = .103) regarding history of *C. diff*; however, female nursing home residents were approximately four years older than males, on average (**Table 14**).

Table 14. Butler Memorial Hospital Nursing Home Patient Encounters (In and Outpatient) by Gender and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	1,471	15.4	8,070	84.6	9,541	100.0	81.33	9.9
Male	761	16.5	3,856	83.5	4,617	100.0	77.29	11.3
Total	2,232	15.8	11,926	84.2	14,158	100.0	80.01	10.5

$\chi^{(1)} = 2.657$, p = .103

Table 15 shows that a majority of the 54,789 patient encounters previously tested for *C. diff* were White (48,813) with 44,053 (90.2%) having no history of *C. diff* and 4,760 (9.8%) having

a history of *C. diff*. Blacks, or African Americans, had the second highest number of encounters (248), of which 235 (94.8%) had no history of *C. diff* and 13 (5.2%) had a prior history of *C. diff*.

Table 15. Butler Memorial Hospital Patient Encounters (In and Outpatient) over Age 18 by Race and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)

	History of C. diff		No History of C. diff		Total	
	N	%	N	%	N	%
White	4,760	9.8	44,053	90.2	48,813	100.0
Black or African American	13	5.2	235	94.8	248	100.0
Asian	6	10.9	49	89.1	55	100.0
Hispanic	4	8.5	43	91.5	47	100.0
Other	5	6.8	68	93.2	73	100.0
Total*	5,980	10.9	48,809	89.1	54,789	100.0

* 4,361 patient encounters' races are unknown or missing

Tables 16 and **17** show the ranking of the Major Diagnostic Categories (MDCs) among Butler County Residents (inpatients and outpatients) over age 18 with a previous positive history of *C. diff*. Each of the 25 Major Diagnostic Categories correspond to a specific organ system and are based on ICD-9 CM codes. **Table 16** displays MDCs for Butler County Encounters while **Table 17** shows MDCs for Butler County primary visits. Each are divided into inpatients and outpatients. Among both encounters and primary visits (among both inpatients and outpatients), the top MDC is Diseases and Disorders of the Digestive System. In **Table 16, t**here is a much higher proportion of those with Diseases and Disorders of the Digestive System among both inpatients and outpatients than the rest of the MDCs – 30.5% for inpatients and 70.7% for outpatients. Similarly, in **Table** 17, there is a higher proportion of those with Diseases and Disorders of the Digestive System among both inpatients and outpatients – 29.5% for inpatients and 72.8% for outpatients. This higher proportion of encounters and individuals with this MDC may be because the data for this study was queried based on a history of *C. diff*, which is a disease of the digestive system.

Table 16. Major Diagnostic Categories (MDCs) among Butler County Residents (Inpatients and Outpatients) (Patient Encounters) Over 18 with a Positive History of *C. diff* (N = 5,980)

	Inpatient N = 1,735	**Outpatient N = 4,245**
	MDC (N, %)	*MDC (N, %)*
1	Digestive system* (529, 30.5%)	Digestive System* (3,000, 70.7%)
2	Infectious and parasitic diseases, systemic or unspecified sites (172, 9.9%)	Factors influencing health status and other contacts with health services (209, 4.9%
3	Respiratory system* (159, 9.2%)	Circulatory system* (84, 2.0%)
4	Circulatory system* (157, 9.0%)	Endocrine, nutritional, and metabolic diseases and disorders (75, 1.8%)
5	Factors influencing health status and other contacts with health services (149, 8.6%)	Infectious and parasitic diseases, systemic or unspecified sites (59, 1.4%)
6	Kidney and urinary tract* (121, 7.0%)	Respiratory system* (57, 1.3%)
7	Endocrine, nutritional, and metabolic diseases and disorders (58, 3.3%)	Blood, blood forming organs, immunological disorders* (55, 1.3%)
8	Blood, blood forming organs, immunological disorders* (46, 2.7%)	Kidney and urinary tract* (48, 1.1%)
9	Musculoskeletal system and connective tissues* (41, 2.4%)	Nervous system* (32, 0.8%)
10	Hepatobiliary system and pancreas* (32, 1.8%)	Musculoskeletal system and connective tissues* (24, 0.6%)
11	Nervous system* (28, 1.6%)	Hepatobiliary system and pancreas* (15, 0.4%)
12	Mental diseases and disorders (28, 1.6%)	Skin, subcutaneous tissue, and breast* (12, 0.3%)
13	Skin, subcutaneous tissue, and breast* (21, 1.2%)	Ear, nose, mouth, and throat* (11, 0.3%)
14	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (11, 0.6%)	Mental diseases and disorders (9, 0.2%)
15	Alcohol/drug use and alcohol/ drug induced organic mental disorders (5, 0.3%)	Female reproductive system* (8, 0.2%)
16	Injuries, poisonings, and toxic effects of drugs (5, 0.3%)	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (7, 0.2%)
17	Ear, nose, mouth, and throat* (4, 0.2%)	Male reproductive system* (2, 0.0%)
18	Female reproductive system* (3, 0.2%)	Injuries, poisonings, and toxic effects of drugs (2, 0.0%)
19	Pregnancy, childbirth, and the puerperium (3, 0.2%)	Pregnancy, childbirth, and the puerperium (2, 0.0%)
20	Male reproductive system* (1, 0.1%)	Alcohol/drug use and alcohol/ drug induced organic mental disorders (1, 0.0%)

*Name begins with "Diseases and Disorders of the"

Table 17. Major Diagnostic Categories (MDCs) among Butler County Residents (Inpatients and Outpatients) (Primary Visits) Over 18 with a Positive History of *C. diff* (N = 2,574)

	Inpatient N = 648	**Outpatient N = 1,926**
	MDC (N, %)	*MDC (N, %)*
1	Digestive system* (191, 29.5%)	Digestive system* (1,403, 72.8%)
2	Infectious and parasitic diseases, systemic or unspecified sites (69, 10.6%)	Factors influencing health status and other contacts with health services (74, 3.8%)
3	Respiratory system* (65, 10,0%)	Endocrine, nutritional, and metabolic diseases and disorders (27, 1.4%)
4	Circulatory system* (54, 8.3%)	Circulatory system* (22, 1.1%)
5	Kidney and urinary tract* (48, 7.4%)	Kidney and urinary tract* (18, 0.9%)
6	Factors influencing health status and other contacts with health services (43, 6.6%)	Blood, blood forming organs, immunological disorders* (16, 0.8%)
7	Nervous system* (18, 2.8%)	Infectious and parasitic diseases, systemic or unspecified sites (16, 0.8%)
8	Endocrine, nutritional, and metabolic diseases and disorders (16, 2.5%)	Respiratory system* (10, 0.5%)
9	Musculoskeletal system and connective tissue* (15, 2.3%)	Nervous system* (8, 0.4%)
10	Mental diseases and disorders (15, 2.3%)	Musculoskeletal system and connective tissue* (7, 0.4%)
11	Hepatobiliary system and pancreas* (13, 2.0%)	Skin, subcutaneous tissue, and breast* (5, 0.3%)
12	Skin, subcutaneous tissue, and breast* (10, 1.5%)	Mental diseases and disorders (5, 0.3%)
13	Blood, blood forming organs, immunological disorders* (8, 1.2%)	Hepatobiliary system and pancreas* (4, 0.2%)
14	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (4, 0.6%)	Ear, nose, mouth, and throat* (3, 0.2%)
15	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (3, 0.5%)	Female reproductive system (2, 0.1%)
16	Injuries, poisonings, and toxic effects of drugs (3, 0.5%)	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (2, 0.1%)
17	Pregnancy, childbirth, and the puerperium (2, 0.3%)	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (1, 0.1%)
18	Ear, nose, mouth, and throat* (1, 0.2%)	Male reproductive system* (1, 0.1%)
19	Female reproductive system* (1, 0.2%)	Injuries, poisonings, and toxic effects of drugs (1, 0.1%)
20	Male reproductive system* (1, 0.2%)	Pregnancy, childbirth, and the puerperium (1, 0.1%)

*Name begins with “Diseases and Disorders of the”

4.3 CLOSTRIDIUM DIFFICILE TEST RESULTS

The follow-up period (1997- March 2017) consisted of 34,879 inpatient and outpatient encounters who were previously tested for *C. diff* in the capture phase (1985-1997) and then subsequently tested in the follow-up period, as shown in **Table 18.** Among inpatients who were tested, 9,775 (88.2%) had no *C. diff* and 1,307 (11.8%) had a positive *C. diff* test while among outpatients, there were 19,878 (83.5%) and 3,919 (16.5%) with negative and positive results, respectively. Almost five percent more of outpatients tested positive for *C. diff* during the follow-up period than inpatients. A Chi-Square Test of Independence shows a higher-than-expected percentage of positive *C. diff* test results among outpatients than inpatients during the follow-up period (p = .000).

Table 18. Butler Memorial Hospital Patient Encounters over Age 18 by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Inpatient	1,307	11.8	9,775	88.2	11,082	100.0	69.7	15.5
Outpatient	3,919	16.5	19,878	83.5	23,797	100.0	69.3	19.6
Total	5,226	15	29,653	85	34,879	100.0	69.4	18.4

$\chi^{(1)} = 129.702$, p = .000

Tables 19-21 show inpatient and outpatient encounters who were tested for *Clostridium difficile* during the follow-up period (1997-March 2017). **Table 19** shows encounters (in and outpatient) aged 18-64. In this age group, inpatient and outpatient *C. diff* test results were similar (p = .330) regarding both positive and negative test results. Among inpatient encounters, 3,205 (90.8%) had a negative test result while 324 (9.2%) had a positive test result. Similarly, among

outpatient encounters, 7,351 (90.2%) had a negative *C. diff* test result and 795 (9.8%) had a positive test result.

Table 19. Butler Memorial Hospital Patient Encounters Ages 18-64 by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Inpatient	324	9.2	3,205	90.8	3,529	100.0	51.0	10.9
Outpatient	795	9.8	7,351	90.2	8,146	100.0	45.9	13.1
Total	1,119	9.6	10,556	90.4	11,675	100.0	47.5	12.7

$\chi^{(1)} = .950$, p = .330

While results were similar among those aged 18-64, there was higher percentage of outpatient encounters who tested positive for *C. diff* among those aged 65+ and among nursing home residents (**Tables 20** and **21**). Among inpatient encounters aged 65+, there were 983 (13%) positive *C. diff* test results and 3,124 (20%) among outpatients, a seven percent difference. The number of positive test results among outpatients was higher than expected, based on a Chi-Square Test of Independence (p =.000).

Table 20. Butler Memorial Hospital Patient Encounters Ages 65+ by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Inpatient	983	13.0	6,570	87.0	7,553	100.0	78.4	7.6
Outpatient	3,124	20.0	12,527	80.0	15,651	100.0	81.4	8.1
Total	4,107	17.7	19,097	82.3	23,204	100.0	80.5	8.1

$\chi^{(1)} = 168.720$, p = .000

Table 21. Butler Memorial Hospital Nursing Home Patient Encounters by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Inpatient	391	14.8	2,251	85.2	2,642	100.0	77.7	10.8
Outpatient	1,869	22.3	6,527	77.7	8,396	100.0	81.3	10.5
Total	2,260	20.5	8,778	79.5	11,038	100.0	80.5	10.6

$\chi^{(1)} = 68.708$, p = .000

Table 22 shows *C. diff* test results among patient encounters in the follow-up period based on two age groups: 18-64 and 65+. Of the 34,879 tested for *C. diff* in the follow-up phase, 10,556 (90.4%) aged 18-64 tested negative for *C. diff* and 1,119 (9.6%) had a positive test. Among those 65+, 19,097 (82.3%) tested negative for *C. diff* and 4,107 (17.7%) tested positive. The percentage of encounters aged 65+ who tested positive for *C. diff* during the follow-up period was almost twice as high as those aged 18-64 who tested positive in the same period (p = .000).

Table 22. Butler Memorial Hospital Patient Encounters (In and Outpatient) Over Age 18 by Age Group (18-64 and 65+) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
18-64	1,119	9.6	10,556	90.4	11,675	100.0	47.5	12.7
65+	4,107	17.7	19,097	82.3	23,204	100.0	80.5	8.1
Total	5,226	15	29,653	85	34,879	100.0	69.4	18.4

$\chi^{(1)} = 401.530$, p = .000

Among females, 18,936 (85.3%) had a negative *C. diff* test result during the follow-up period while 3,268 (14.7%) had positive test. Similarly, 10,717 (84.6%) males had a negative *C. diff* test result and 1,958 (15.4%) tested positive for *C. diff* (**Table 23**). There is no relationship between gender and *C. diff* test results during the follow-up period (p = .066).

Table 23. Butler Memorial Hospital Patient Encounters (In and Outpatient) Over Age 18 by Gender and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	3,268	14.7	18,936	85.3	22,204	100.0	70.4	18.7
Male	1,958	15.4	10,717	84.6	12,675	100.0	67.6	17.8
Total	5,226	15	29,653	85	34,879	100.0	69.4	18.4

$\chi^{(1)} = 3.372$, p = .066

There was no difference in the number of female versus male encounters who tested positive for *C. diff* during the follow-up period among those aged 18-64 (**Table 24**); however,

among those 65 and older, there were slightly more males compared to females who tested positive (p = .003) (**Table 25**). Also, females who tested for *C. diff* were, on average, approximately two years older than males (**Table 25**).

Table 24. Butler Memorial Hospital Patient Encounters (In and Outpatient) Ages 18-64 by Gender and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	666	9.5	6,372	90.5	7,038	100.0	47.1	12.9
Male	453	9.8	4,184	90.2	4,637	100.0	48.0	12.5
Total	1,119	9.6	10,556	90.4	11,675	100.0	47.5	12.7

$\chi^{(1)} = .303$, p = .582

Table 25. Butler Memorial Hospital Patient Encounters (In and Outpatient) Ages 65+ by Gender and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	2,602	17.2	12,564	82.8	15,166	100.0	81.2	8.1
Male	1,505	18.7	6,533	81.3	8,038	100.0	79.0	7.7
Total	4,107	17.7	19,097	82.3	23,204	100.0	80.5	8.1

$\chi^{(1)} = 8.853$, p = .003

Table 26 shows nursing home patients (encounters) who were tested for *C. diff* during the follow-up period. Among females, 5,983 (80.2%) tested negative for *C. diff* and 1,480 (19.8%) tested positive. There were 2,795 (78.2%) males who tested negative and 780 (21.8%) who tested positive. In addition, the percentage of males and females who tested positive is much larger than that reported in **Table 24**, most likely due to the higher age of the nursing home population.

Table 26. Butler Memorial Hospital Nursing Home Patient Encounters (In and Outpatient) by Gender and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total			
	N	%	N	%	N	%	$\bar{x}$	SD
Female	1,480	19.8	5,983	80.2	7,463	100.0	81.8	10.1
Male	780	21.8	2,795	78.2	3,575	100.0	77.8	11.3
Total	2,260	20.5	8,778	79.5	11,038	100.0	80.5	10.6

$\chi^{(1)} = 5.861$, p = .015

Table 27 shows that a majority of the 34,879 patient encounters tested for *C. diff* in the follow-up period were White (29,413) with 25,456 (86.5%) having a negative *C. diff* test and 3,957 (13.5%) having *C. diff*. Black, or African Americans, had the second highest number of encounters (150) of which 132 (88%) had a negative *C. diff* test and 18 (12%) had a positive *C. diff* test.

Table 27. Butler Memorial Hospital Patient Encounters (In and Outpatient) Over Age 18 by Race and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

	C. diff		No C. diff		Total	
	N	%	N	%	N	%
White	3,957	13.5	25,456	86.5	29,413	100.0
Black/ African American	18	12	132	88	150	100.0
Asian	4	11.4	31	88.6	35	100.0
Hispanic	5	16.7	25	83.3	30	100.0
Other	4	12.1	29	87.9	33	100.0
Total*	5,226	15.0	29,653	85.0	34,879	100.0

* 3,980 patient encounters' races are unknown or missing

Tables 28 and **29** show the ranking of the Major Diagnostic Categories (MDCs) among Butler County Residents (inpatients and outpatients) over age 18 with a positive *C. diff* test result in the follow up period (1997-March 2017). **Table 28** displays MDCs for Butler County Encounters while **Table 29** shows MDCs for Butler County primary visits. Each are divided into inpatients and outpatients. Among both encounters and primary visits (among both inpatients and outpatients), the top MDC is Diseases and Disorders of the Digestive System. In **Table 28,** there is a much higher proportion of those with Diseases and Disorders of the Digestive System among both inpatients and outpatients than the rest of the MDCs – 32.6% for inpatients and 71.4% for outpatients. Similarly, in **Table 29**, there is a higher proportion of those with Diseases and Disorders of the Digestive System among inpatients and outpatients – 30.3% for inpatients and 74.0% for outpatients. Again, this higher proportion of encounters and individuals with this MDC

may be because the data for this study was queried based on a history of *C. diff*, which is a disease of the digestive system.

Table 28. Major Diagnostic Categories (MDCs) among Butler County Residents (Inpatients and Outpatients) (Patient Encounters) Over 18 with a Positive *C. diff* Test between 1997-March 2017 (N = 5,226)

	Inpatient N = 1,307	**Outpatient N = 3,919**
	MDC (N, %)	*MDC (N, %)*
1	Digestive system* (426, 32.6%)	Digestive system* (2,798, 71.4%)
2	Infectious and parasitic diseases, systemic or unspecified sites (135, 10.3%)	Factors influencing health status and other contacts with health services (189, 4.8%)
3	Respiratory system* (121, 9.3%)	Circulatory system* (76, 1.9%)
4	Factors influencing health status and other contacts with health services (120, 9.2%)	Infectious and parasitic diseases, systemic or unspecified sites (63, 1.6%)
5	Circulatory system* (113, 8.6%)	Endocrine, nutritional, and metabolic diseases and disorders (54, 1.4%)
6	Kidney and urinary tract* (60, 4.6%)	Blood, blood forming organs, immunological disorders* (50, 1.3%)
7	Endocrine, nutritional, and metabolic diseases and disorders (39, 3.0%)	Kidney and urinary tract* (49, 1.3%)
8	Musculoskeletal system and connective tissue* (27, 2.1%)	Respiratory system* (49, 1.3%)
9	Mental diseases and disorders (25, 1.9%)	Nervous system* (27, 0.7%)
10	Blood, blood forming organs, immunological disorders* (21, 1.6%)	Musculoskeletal system and connective tissue* (25, 0.6%)
11	Nervous system* (15, 1.1%)	Hepatobiliary system and pancreas* (10, 0.3%)
12	Skin, subcutaneous tissue, and breast* (15, 1.1%)	Ear, nose, mouth, and throat* (9, 0.2%)
13	Hepatobiliary system and pancreas* (14, 1.1%)	Skin, subcutaneous tissue, and breast* (9, 0.2%)
14	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (12, 0.9%)	Mental diseases and disorders (9, 0.2%)
15	Female reproductive system* (3, 0.2%)	Female reproductive system* (7, 0.2%)
16	Male reproductive system (3, 0.2%)	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (6, 0.2%)
17	Injuries, poisonings, and toxic effects of drugs (3, 0.2%)	Injuries, poisonings, and toxic effects of drugs (4, 0.1%)
18	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (2, 0.2%)	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (1, 0.0%)
19	Ear, nose, mouth, and throat (2, 0.2%)	Male reproductive system* (1, 0.0%)
20	----------	Pregnancy, childbirth, and the puerperium (1, 0.0%)

*Name begins with “Diseases and Disorders of the”

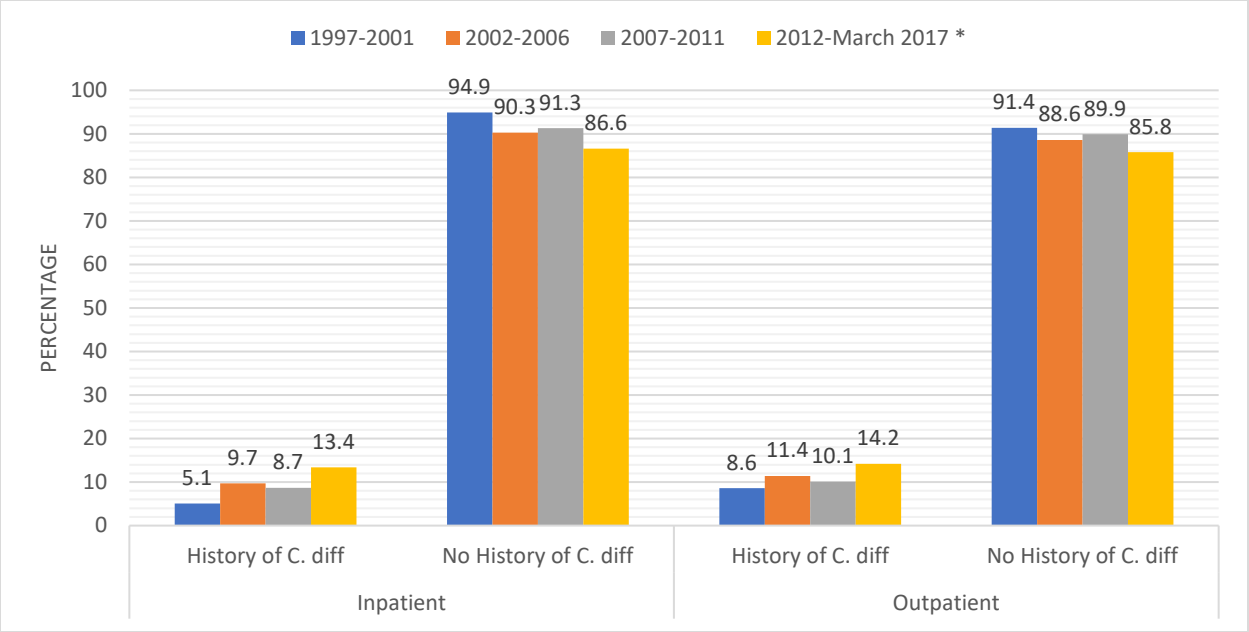
Table 29. Major Diagnostic Categories (MDCs) among Butler County Residents (Inpatients and Outpatients) (Primary Visits) Over 18 with a Positive *C. diff* Test between 1997-March 2017 (N = 2,507)

	Inpatient N = 601	**Outpatient N = 1,906**
	MDC (N, %)	*MDC (N, %)*
1	Digestive system* (182, 30.3%)	Digestive system* (1,410, 74.0%)
2	Respiratory system* (72, 12.0%)	Factors influencing health status and contacts with health services (71, 3.7%)
3	Infectious and parasitic diseases, systemic or unspecified sites (58, 9.7%)	Circulatory system* (24, 1.3%)
4	Circulatory system* (48, 8.0%)	Kidney and urinary tract* (19, 1.0%)
5	Factors influencing health status and other contacts with health services (44, 7.3%)	Endocrine, nutritional, and metabolic diseases and disorders (19, 1.0%)
6	Kidney and urinary tract* (28, 4.7%)	Infectious and parasitic diseases, systemic or unspecified sites (17, 0.9%)
7	Endocrine, nutritional, and metabolic diseases and disorders (17, 2.8%)	Blood, blood forming organs, immunological disorders* (16, 0.8%)
8	Musculoskeletal system and connective tissue* (15, 2.5%)	Respiratory system* (10, 0.5%)
9	Mental diseases and disorders (13, 2.2%)	Musculoskeletal system and connective tissue* (8, 0.4%)
10	Nervous system* (8, 1.3%)	Nervous system* (7, 0.4%)
11	Blood, blood forming organs, immunological disorders* (6, 1.0%)	Hepatobiliary system and pancreas* (4, 0.2%)
12	Hepatobiliary system and pancreas* (6, 1.0%)	Skin, subcutaneous tissue, and breast* (4, 0.2%)
13	Skin, subcutaneous tissue, and breast* (6, 1.0%)	Female reproductive system* (3, 0.2%)
14	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (4, 0.7%)	Injuries, poisonings, and toxic effects of drugs (3, 0.2%)
15	Female reproductive system* (3, 0.5%)	Mental diseases and disorders (3, 0.2%)
16	Injuries, poisonings, and toxic effects of drugs (3, 0.5%)	Ear, nose, mouth, and throat (2, 0.1%)
17	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (2, 0.3%)	Alcohol/ drug use and alcohol/ drug induced organic mental disorders (1, 0.1%)
18	Ear, nose, mouth, and throat* (1, 0.2%)	Male reproductive system* (1, 0.1%)
19	Male reproductive system* (1, 0.2%)	Myeloproliferative diseases and disorders, poorly differentiated neoplasm (1, 0.1%)
20	----------	Pregnancy, childbirth, and the puerperium (1, 0.1%)

*Name begins with "Diseases and Disorders of the"

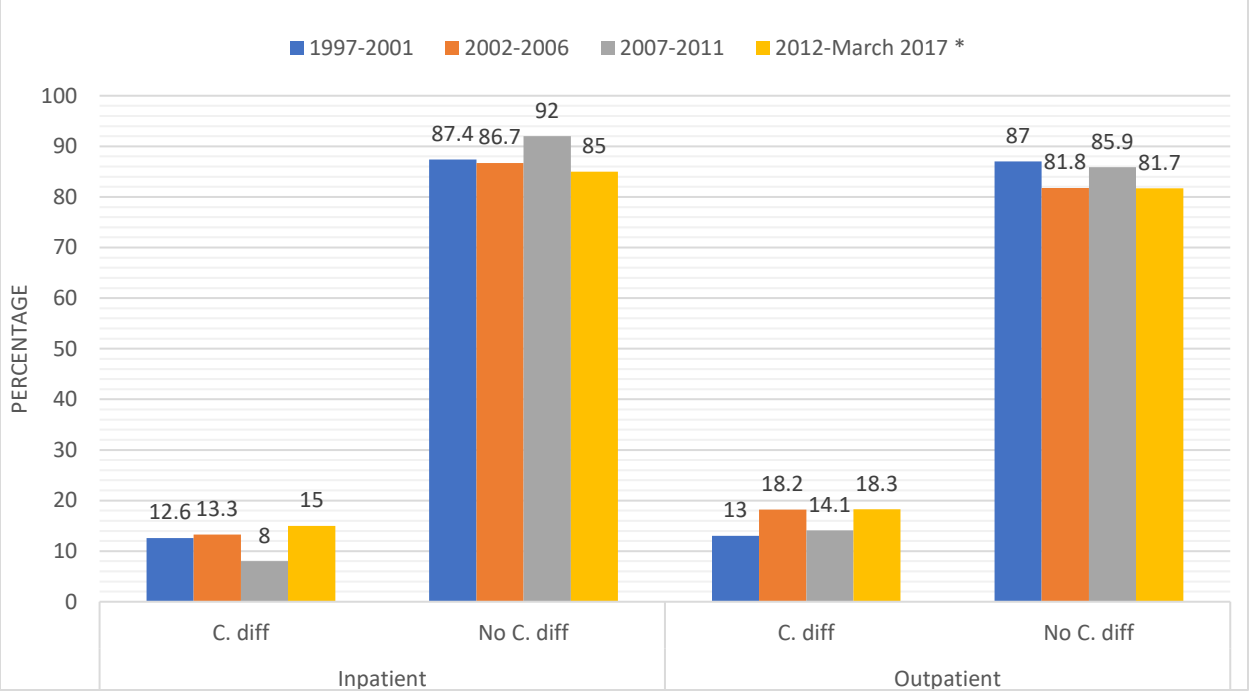
4.4 TRENDS OVER TIME

Tables 30 and **31** and **Figures 4** and **5** show trends over time by prior history of *Clostridium difficile* during the 1985-1997 capture phase and subsequent *C. diff* test results during the 1997-March 2017 follow-up phase, respectively, for encounters over the age of 18. The time periods are divided into four-year-intervals: 1997-2001, 2002-2006, 2007-2011, and 2012-present. Among the 54,789 patient encounters previously tested in the capture phase, 17,937 were inpatient and 36,852 were outpatient. The follow-up period consisted of 34,879 patient encounters of which 11,082 are inpatient and 23,797 are outpatient. These are individuals who not only have a prior *C. diff* testing history, but a testing history for the 20-year follow-up period as well.



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 4. Percent Butler Memorial Hospital Patient Encounters over Age 18 over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 5. Percent Butler Memorial Hospital Patient Encounters over Age 18 over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result During Follow-up Period (1997-March 2017) (Butler County Residents Only)

Considering the number and proportion of encounters with a positive history of *C. diff* (**Figure 4**) over time and those with a subsequent positive *C. diff* test result, (**Figure 5**), the trends are very similar, both fluctuating in the same direction between time periods in both inpatients and outpatients. There is an overall increasing trend in the percentage of encounters with a positive history of *C. diff* over time ranging from 5.1% (129 encounters) who previously tested positive for *C. diff* among inpatients in the 1997-2001 period to 13.4% (608 encounters) who previously tested positive among inpatients in the 2012-present period. Similarly, among outpatients, the percentage of encounters with a positive history of *C. diff* increases over time from 8.6% (291 encounters) in the 1997-2001 period to 14.2% (1,463 encounters) in the 2012-present period.

Among those tested in the follow-up period, there is a similar increasing trend over time (**Figure 5**). The same fluctuation with a general increase over time exists among inpatient encounters in the follow-up period with 138 (12.6%) positive test results in the 1997-2001 period, increasing to 463 (15%) in the 2012-present period. Among outpatient encounters, 13% (274 encounters) tested positive for *C. diff* in the 1997-2001 follow-up period, increasing to 18.3% (1,301) who tested positive during the 2012-present period. **Figures 4** and **5** show a higher percentage of outpatients testing positive for *C. diff* as previously shown.

Among inpatient encounters in the capture phase, mean age decreased over the four time periods from 71.16 in 1997-2001 to 69.52 in 2012-March 2017. On the other hand, mean age increased slightly among outpatient encounters in the capture phase over the four times periods from 66.30 in 1997-2001 to 67.34 in 2012-March 2017 (**Table 30**). Among both inpatient and outpatient encounters in the follow-up phase (1997-March 2017), the mean age remained relatively stable (**Table 31**) with a slight increase in the 2002-2006 and 2007-2011 years among both inpatient and outpatient encounters. While **Tables 30** and **31** include all encounters ages 18 and

older, the results suggest that an aging cohort is not the cause of the increase in a positive history of *C. diff* and positive *C. diff* test results during the follow-up period. Another possible explanation for the increase between the 2007- 2011 and 2012-March 2017 time periods is the switch from the enzyme immunoassay testing method to the molecular testing method, which is a more sensitive test and could lead to higher proportions of positive test results and thus higher proportions of encounters with a positive *C. diff* test.

A Chi-Square Test of Independence (**Table 30**) indicates higher-than-expected proportions of positive history of *C. diff* in the 2012-March 2017 period while all other time periods have lower-than-expected proportions ($p = .000$). In the follow-up period (**Table 31**), the 1997-2001, 2002-2006, and 2012-March 2017 periods had higher than expected numbers of positive *C. diff* test results while the 2007-2011 period had lower-than expected numbers of positive *C.diff* test results among both inpatients and outpatients ($p = .000$).

Table 30. Butler Memorial Hospital Patient Encounters over Age 18 over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only) (N = 54,789)

		History of C. diff		No History of C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	129	5.1	2,393	94.9	2,522	100.0	71.2	14.8
	2002-2006	517	9.7	4,834	90.3	5,351	100.0	71.2	15.3
	2007-2011	481	8.7	5,031	91.3	5,512	100.0	70.9	15.3
	2012- March 2017*	608	13.4	3,944	86.6	4,552	100.0	69.5	15.4
	Total	**1,735**	**9.7**	**16,202**	**90.3**	**17,937**	**100.0**	**70.9**	**15.3**
Outpatient									
	1997-2001	291	8.6	3,098	91.4	3,389	100.0	66.3	18.2
	2002-2006	1,358	11.4	10,598	88.6	11,956	100.0	70.2	16.3
	2007-2011	1,133	10.1	10,050	89.9	11,183	100.0	70.2	17.4
	2012-March 2017*	1,463	14.2	8,861	85.8	10,324	100.0	67.3	18.5
	Total	**4,245**	**11.5**	**32,607**	**88.5**	**36,852**	**100.0**	**69.0**	**17.5**
Total	*Of each column's N*	**5,980**	**10.9**	**48,809**	**89.1**	**54,789**	**100.0**	**69.6**	**16.8**

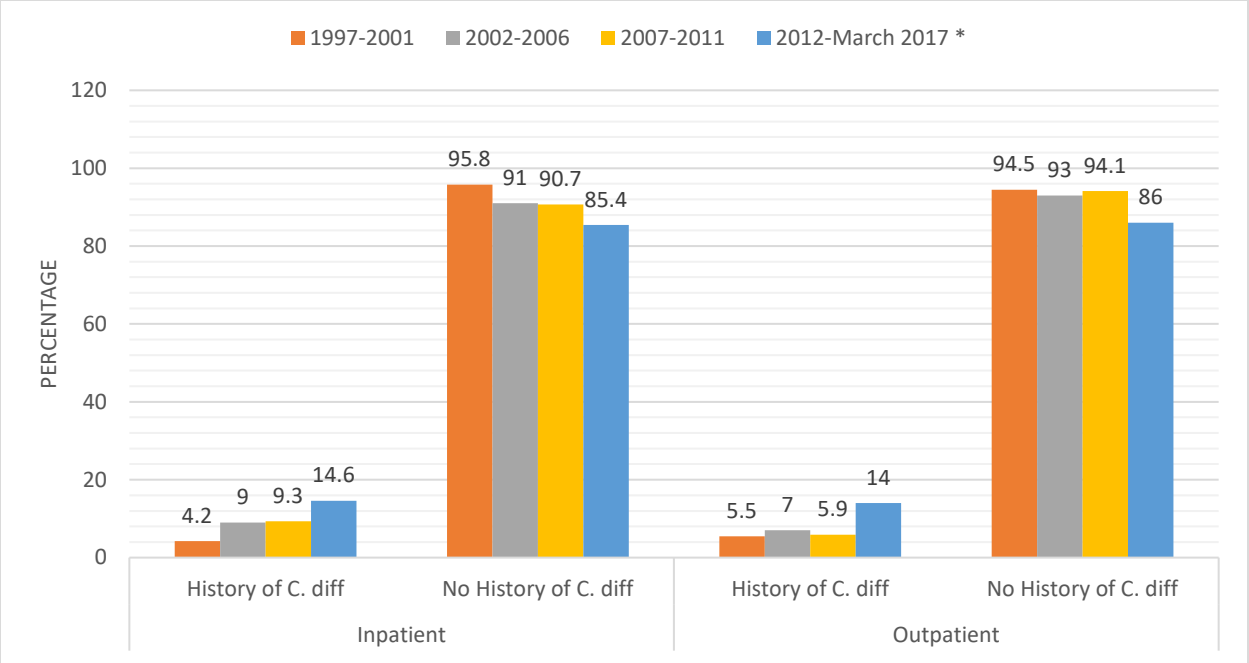
Inpatient $\chi^{(3)} = 136.322$, p = .000, *Outpatient* $\chi^{(3)} = 121.253$, p = .000, *Total* $\chi^{(3)} = 253.378$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Table 31. Butler Memorial Hospital Patient Encounters over Age 18 over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only) (N = 34,879)

		C. diff		No C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	138	12.6	960	87.4	1,098	100.0	69.8	15.2
	2002-2006	415	13.3	2,705	86.7	3,120	100.0	70.2	15.7
	2007-2011	291	8.0	3,416	92	3,707	100.0	70.2	15.4
	2012- March 2017*	463	15.0	2,694	85	3,157	100.0	68.7	15.6
	Total	**1,307**	**12.0**	**9,775**	**88**	**11,082**	**100.0**	**69.7**	**15.5**
Outpatient									
	1997-2001	274	13.0	1,831	87	2,105	100.0	66.0	21.1
	2002-2006	1,273	18.2	5,722	81.8	6,995	100.0	71.7	18.8
	2007-2011	1,071	14.1	6,513	85.9	7,584	100.0	70.2	19.5
	2012- March 2017*	1,301	18.3	5,812	81.7	7,113	100.0	66.9	19.8
	Total	**3,919**	**16.5**	**19,878**	**83.5**	**23,797**	**100.0**	**69.3**	**19.6**
Total	*Of each column's N*	**5,226**	**15.0**	**29,653**	**85**	**34,879**	**100.0**	**69.4**	**18.4**

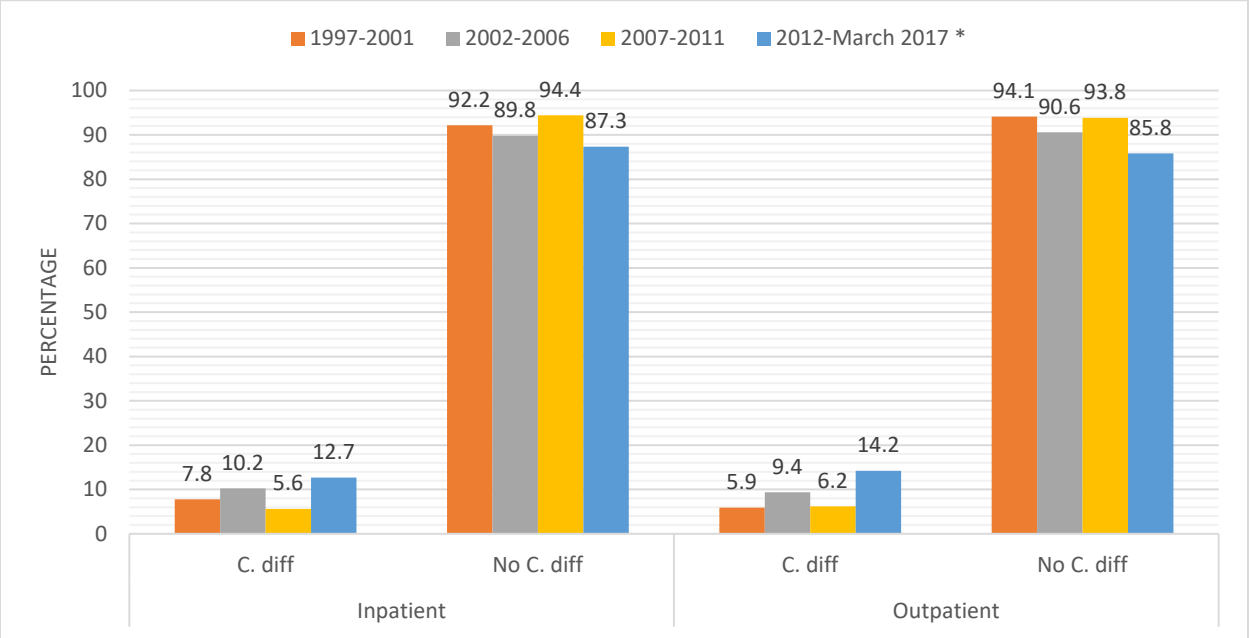
Inpatient $\chi^{(3)} = 87.901$, p = .000, *Outpatient* $\chi^{(3)} = 80.979$, p = .000, *Total* $\chi^{(3)} = 148.762$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Tables 32 and **33** and **Figures 6** and **7** show trends over time by prior history of *Clostridium difficile* during the 1985-1997 capture phase and subsequent *C. diff* test results during the 1997-March 2017 follow-up phase, respectively for encounters ages 18-64. Among the 17,950 18-64-year-olds (encounters) previously tested in the capture phase, 5,286 were inpatient and 12,664 were outpatient. The follow-up period consisted of 11,675 patient encounters aged 18-64 of which 3,529 were inpatient and 8,146 were outpatient.



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 6. Percent Butler Memorial Hospital Patient Encounters Ages 18-64 over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 7. Percent Butler Memorial Hospital Patient Encounters Ages 18-64 over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

Considering the number and proportion of encounters with a positive history of *C. diff* (**Figure 6**) over time and those with a subsequent positive *C. diff* test result, (**Figure 7**), there is an overall increasing trend in the percentage of encounters with a positive history of *C. diff* over time ranging from 4.2% (27 encounters) who previously tested positive for *C. diff* among inpatients in the 1997-2001 time period to 14.6% (215 encounters) who previously tested positive among inpatients in the 2012-present period. Similarly, among outpatients, the percentage of encounters with a positive history of *C. diff* increased over time from 5.5% (77 encounters) in the 1997-2001 period to 14.0% (546 encounters) in the 2012-present period (**Table 32**).

Among patient encounters with in and outpatients 18-64 tested in the follow-up period, there is a similar increasing trend over time (**Figure 7**). The same fluctuation with a general increase over time exists among inpatient encounters in the follow-up period with 23 (7.8%) positive test results in the 1997-2001 period, increasing to 137 (12.7%) in the 2012-present period. Among outpatient encounters, 5.9% (49 encounters) tested positive for *C. diff* in the 1997-2001 follow-up period, increasing to 14.2% (405) who tested positive during the 2012-present period.

Among inpatient encounters in the capture phase, mean age increased slightly over the four time periods from 50.40 in the 1997-2001 period to 51.53 in the 2012-March 2017 period. Among outpatient encounters in the capture phase over the four times periods, mean age fluctuated from 47.96 in 1997-2001 to 50.71 in 2002-2006 to 48.94 in 2007-20011 to 47.83 in 2012-March 2017 (**Table 32**). Among both inpatient and outpatient encounters in the follow-up phase (1997-March 2017), the mean age increased slightly (**Table 33**) from 49.18 in 1997-2001 to 51.17 among inpatients and from 43.01 in 1997-2001 to 46.70 in 2012-March 2017 among outpatients. **Tables 32** and **33** also do not suggest that an aging cohort to be the cause of the increase in a positive history of *C. diff* and positive *C. diff* test results during the follow-up period. The switch in testing

methods from enzyme immunoassay to the molecular testing method may explain the increase in the proportion testing positive between the 2007-20011 and 2012-March 2017 time periods

A Chi-Square Test of Independence (**Table 32**) indicates higher-than-expected proportions of positive history of *C. diff* in the 2012-March 2017 period while all other time periods had lower-than-expected proportions (p = .000). In the follow-up period (**Table 33**), the 2002-2006, and 2012-March 2017 periods had higher than expected numbers of positive *C. diff* test results while the other time periods had lower-than expected numbers of positive *C.diff* test results among inpatients and outpatients (p = .000).

Table 32. Butler Memorial Hospital Patient Encounters Ages 18-64 over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only) (N = 17,950)

		History of C. diff		**No History of C. diff**		**Total**			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	27	4.2	620	95.8	647	100.0	50.4	11.0
	2002-2006	134	9.0	1,348	91.0	1,482	100.0	50.7	11.1
	2007-2011	157	9.3	1,525	90.7	1,682	100.0	51.8	10.5
	2012- March 2017*	215	14.6	1,260	85.4	1,475	100.0	51.5	10.8
	Total	**533**	**10.1**	**4,753**	**89.9**	**5,286**	**100.0**	**51.3**	**10.8**
Outpatient									
	1997-2001	77	5.5	1,311	94.5	1,388	100.0	48.0	12.2
	2002-2006	268	7.0	3,567	93.0	3,835	100.0	50.7	11.6
	2007-2011	210	5.9	3,326	94.1	3,536	100.0	48.9	12.5
	2012- March 2017*	546	14.0	3,359	86.0	3,905	100.0	47.8	13.3
	Total	**1,101**	**8.7**	**11,563**	**91.3**	**12,664**	**100.0**	**49.0**	**12.5**
Total		**1,634**	**9.1**	**16,316**	**90.9**	**17,950**	**100.0**	**49.7**	**12.1**

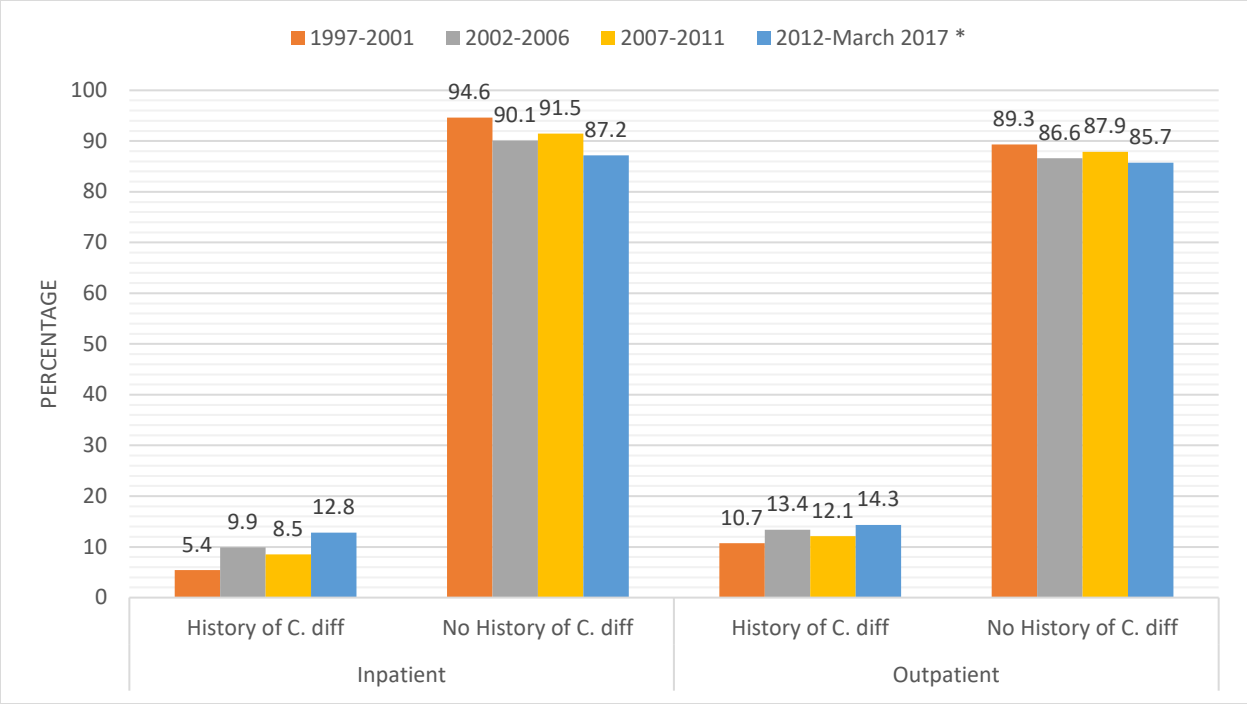
Inpatient $\chi^{(3)} = 60.582$, p = .000, *Outpatient* $\chi^{(3)} = 202.741$, p = .000, *Total* $\chi^{(3)} = 246.790$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Table 33. Butler Memorial Hospital Patient Encounters Ages 18-64 over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only) (N = 11,675)

		C. diff		No C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	23	7.8	273	92.2	296	100.0	49.2	11.2
	2002-2006	96	10.2	849	89.8	945	100.0	50.4	11.1
	2007-2011	68	5.6	1,137	94.4	1,205	100.0	51.9	10.6
	2012-March 2017*	137	12.7	946	87.3	1,083	100.0	51.2	11.0
	Total	**324**	**9.2**	**3,205**	**90.8**	**3,529**	**100.0**	**51.0**	**10.9**
Outpatient									
	1997-2001	49	5.9	783	94.1	832	100.0	43.0	12.3
	2002-2006	191	9.4	1,831	90.6	2,022	100.0	46.3	12.8
	2007-2011	150	6.2	2,282	93.8	2,432	100.0	45.7	13.1
	2012-March 2017*	405	14.2	2,455	85.8	2,860	100.0	46.7	13.5
	Total	**795**	**9.8**	**7,351**	**90.2**	**8,146**	**100.0**	**45.9**	**13.1**
Total		**1,119**	**9.6**	**10,556**	**90.4**	**11,675**	**100.0**	**47.5**	**12.7**

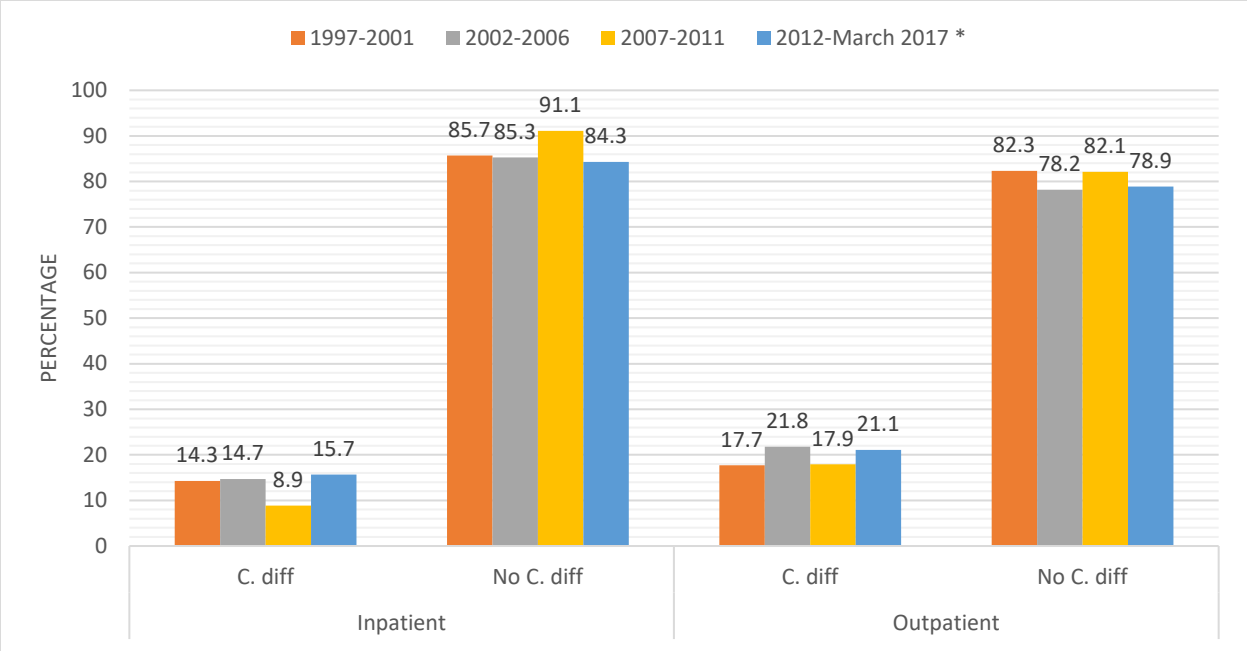
Inpatient $\chi^{(3)} = 35.509$, p = .000, *Outpatient* $\chi^{(3)} = 112.908$, p = .000, *Total* $\chi^{(3)} = 146.268$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Tables 34 and **35** and **Figures 8** and **9** show trends over time by prior history of *Clostridium difficile* during the 1985-1997 capture phase and subsequent *C. diff* test results during the 1997-March 2017 follow-up phase, respectively for encounters ages 65+. Among the 36,839 encounters aged 65 and older previously tested in the capture phase, 12,651 were inpatient and 24,188 were outpatient. The follow-up period consisted of 23,204 patient encounters over age 65 of which 7,553 were inpatient and 15,651 were outpatient.



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 8. Butler Memorial Hospital Patient Encounters Ages 65+ over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 9. Percent Butler Memorial Hospital Patient Encounters Ages 65+ over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

Considering the number and proportion of encounters with a positive history of *C. diff* (**Figure 8**) over time and those with a subsequent positive *C. diff* test result, (**Figure 9**), there was an overall increasing trend in the percentage of encounters with a positive history of *C. diff* over time ranging from 5.4% (102 encounters) who previously tested positive for *C. diff* among inpatients in the 1997-2001 time period to 12.8% (393 encounters) who previously tested positive among inpatients in the 2012-present period. Similarly, among outpatients, the percentage of encounters with a positive history of *C. diff* increased over time from 10.7% (214 encounters) in the 1997-2001 period to 14.3% (917 encounters) in the 2012-present period (**Table 34**).

Among patient encounters with in- and outpatients aged 65 and older tested in the follow-up period, there was a similar increasing trend over time (**Figure 9**). The same fluctuation with a general increase over time existed among inpatient encounters in the follow-up period with 115 (14.3%) positive test results in the 1997-2001 period, increasing to 326 (15.7%) in the 2012-present period. Among outpatient encounters, 17.7% (225 encounters) tested positive for *C. diff* in the 1997-2001 follow-up period, increasing to 21.1% (896) who tested positive during the 2012-present period, an increase of almost 3.5% (**Table 35**).

Among inpatient encounters in the capture phase, mean age remained stable, between 78 and 79-years-old. Among outpatient encounters in the capture phase over the four times periods, mean age stayed between 79 and 80-years-old (**Table 34**). Among inpatients in the follow-up phase (1997-March 2017), the mean age fluctuated between 77 and 78-years-old (**Table 35**) while among outpatients, the mean age decreased very slightly overall from 81.07-years-old in 1997-2001 to 80.41 in 2012-March 2017 (**Table 35**).

A Chi-Square Test of Independence (**Table 34**) indicates higher-than-expected numbers with a positive history of *C. diff* in the 2002-2006 and 2012-March 2017 period while all other

time periods had lower-than-expected proportions among both inpatients and outpatients (p = .000). In the follow-up period (**Table 35**), the 1997-2001, 2002-2006, and 2012-March 2017 periods had higher than expected numbers of positive *C. diff* test results among inpatients while the other time periods had lower-than expected numbers. Among outpatients there were higher numbers of positive test results in the 2002-2006 and 2012-present time periods (p = .000).

Table 34. Butler Memorial Hospital Patient Encounters Ages 65+ over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only) (N = 36,839)

		History of C. diff		No History of C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	102	5.4	1,773	94.6	1,875	100.0	78.3	7.4
	2002-2006	383	9.9	3,486	90.1	3,869	100.0	79.1	7.3
	2007-2011	324	8.5	3,506	91.5	3,830	100.0	79.2	7.7
	2012- March 2017*	393	12.8	2,684	87.2	3,077	100.0	78.1	8.0
	Total	**1,202**	**9.5**	**11,449**	**90.5**	**12,651**	**100.0**	**78.8**	**7.6**
Outpatient									
	1997-2001	214	10.7	1,787	89.3	2,001	100.0	79.0	7.9
	2002-2006	1,090	13.4	7,031	86.6	8,121	100.0	79.4	8.1
	2007-2011	923	12.1	6,724	87.9	7,647	100.0	80.0	8.0
	2012- March 2017*	917	14.3	5,502	85.7	6,419	100.0	79.2	8.4
	Total	**3,144**	**13.0**	**21,044**	**87.0**	**24,188**	**100.0**	**79.5**	**8.2**
Total		**4,346**	**11.8**	**32,493**	**88.2**	**36,839**	**100.0**	**79.3**	**8.0**

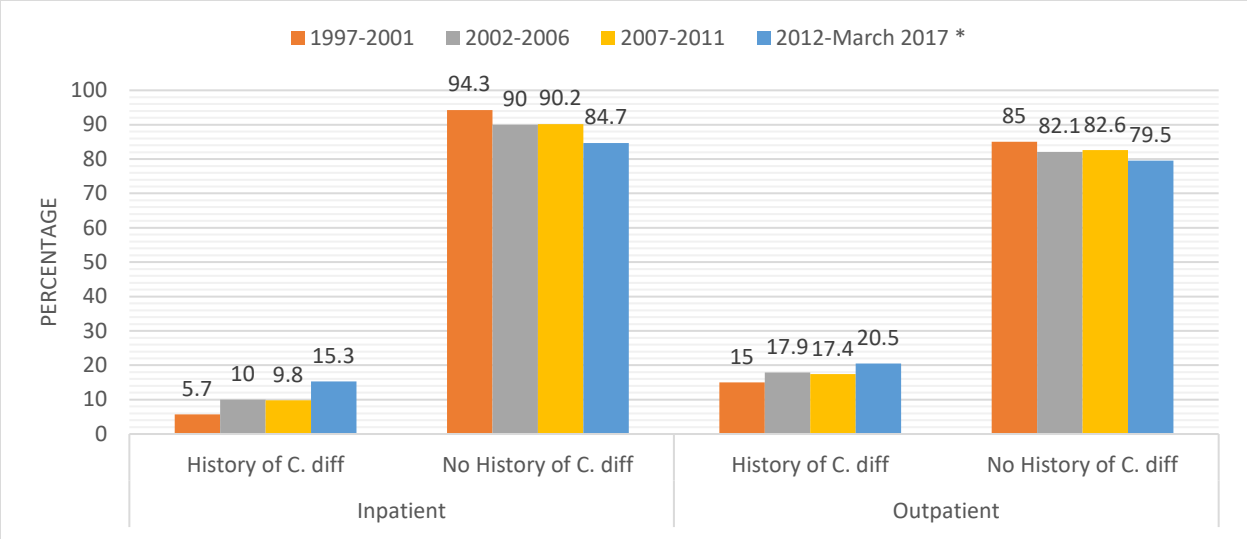
Inpatient $\chi^{(3)} = 79.799$, p = .000, *Outpatient* $\chi^{(3)} = 25.913$, p = .000, *Total* $\chi^{(3)} = 98.234$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Table 35. Butler Memorial Hospital Patient Encounters Ages 65+ over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only) (N = 23,204)

		C. diff		No C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	115	14.3	687	85.7	802	100.0	77.4	7.3
	2002-2006	319	14.7	1,856	85.3	2,175	100.0	78.8	7.4
	2007-2011	223	8.9	2,279	91.1	2,502	100.0	79.0	7.6
	2012-March 2017*	326	15.7	1,748	84.3	2,074	100.0	77.9	7.9
	Total	**983**	**13.0**	**6,570**	**87.0**	**7,553**	**100.0**	**78.4**	**7.6**
Outpatient									
	1997-2001	225	17.7	1,048	82.3	1,273	100.0	81.1	7.8
	2002-2006	1,082	21.8	3,891	78.2	4,973	100.0	82.0	7.8
	2007-2011	921	17.9	4,231	82.1	5,152	100.0	81.8	7.8
	2012-March 2017*	896	21.1	3,357	78.9	4,253	100.0	80.4	8.6
	Total	**3,124**	**20.0**	**12,527**	**80.0**	**15,651**	**100.0**	**81.4**	**8.1**
Total		**4,107**	**17.7**	**19,097**	**82.3**	**23,204**	**100.0**	**80.5**	**8.1**

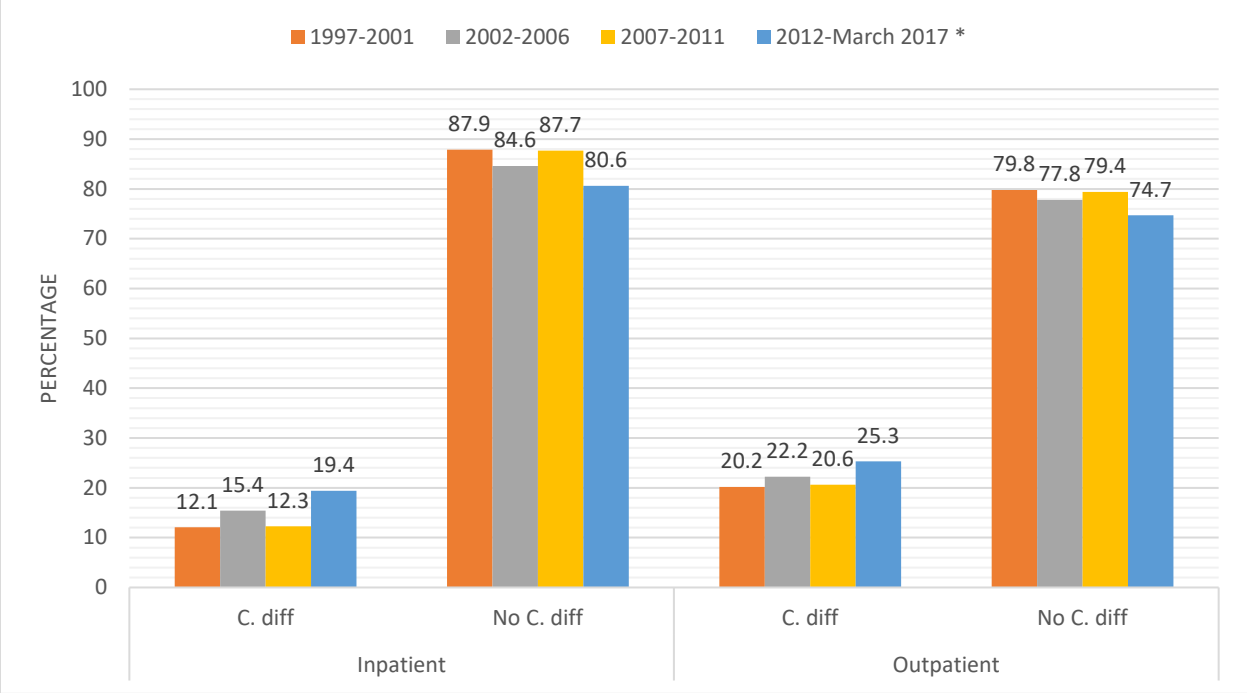
Inpatient $\chi^{(3)} = 57.062$, p = .000, *Outpatient* $\chi^{(3)} = 31.481$, p = .000, *Total* $\chi^{(3)} = 71.329$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Tables 36 and **37** and **Figures 10** and **11** show trends over time by prior history of *Clostridium difficile* during the 1985-1997 capture phase and subsequent *C. diff* test results during the 1997-March 2017 follow-up phase, respectively for nursing home resident encounters. Among the 14,158 patient encounters previously tested in the capture phase, 4,324 were inpatient and 9,834 were outpatient (**Table 36**). The follow-up period consisted of 11,038 patient encounters of which 2,642 were inpatient and 8,396 outpatients (**Table 37**).



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 10. Percent Butler Memorial Hospital Nursing Home Patient Encounters over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only)



*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Figure 11. Percent Butler Memorial Hospital Nursing Home Patient Encounters over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only)

Considering the number and proportion of encounters with a positive history of *C. diff* (**Figure 10**) over time and those with a subsequent positive *C. diff* test result, (**Figure 11**), there was an overall increasing trend in the percentage of nursing home resident encounters with a positive history of *C. diff* over time ranging from 5.7% (31 encounters) who previously tested positive for *C. diff* among inpatients in the 1997-2001 time period to 15.3% (128 encounters) who previously tested positive among inpatients in the 2012-present period. Similarly, among outpatients, the percentage of encounters with a positive history of *C. diff* increased over time from 15% (119 encounters) in the 1997-2001 period to 20.5% (467 encounters) in the 2012-present period (**Table 36**). There was almost a 10% increase among inpatients with a positive history of *C. diff* between 1997-2001 and 2012-March 2017 and a 5% increase among outpatients during the same time. In fact, in the 2012-March 2017 period, there were a higher proportion of outpatients with a history of *C. diff* than inpatients, which suggests that these patients returned to nursing homes with *C. diff* to potentially spread the infection to others.

Among those tested in the follow-up period, there was a similar increasing trend over time (**Figure 11**). A fluctuation with a general increase over time exists among inpatient nursing home encounters in the follow-up period with 29 (12.1%) positive test results in the 1997-2001 period, increasing to 113 (19.4%) in the 2012-present period. Among outpatient encounters, 20.2% (125 encounters) tested positive for *C. diff* in the 1997-2001 follow-up period, increasing to 25.3% (507) who tested positive during the 2012-present period. Again, there was a higher proportion of nursing home resident outpatient encounters testing positive for *C. diff* in the follow-up phase than inpatients.

Among inpatient encounters in the capture phase, mean age increased over the four time periods from 76.77 in 1997-2001 to 78.94 in the 2012-March 2017 period. Mean age also increased

slightly among outpatient encounters in the capture phase over the four times periods from 78.09 in 1997-2001 to 81.52 in 2012-March 2017 (**Table 36**). Among both inpatient and outpatient encounters in the follow-up phase (1997-March 2017), the mean age increased over the time periods (**Table 37**) from 76.63 (1997-2001) to 78.54 (2012-March 2017) among inpatients and from 79 (1997-2001) to 81.88 (2012-March 2017) among outpatients. **Tables 36** and **37** indicate a slight aging of the cohort, which may contribute to the increase in the proportion of positive test results.

A Chi-Square Test of Independence (**Table 36**) indicates higher-than-expected proportions of positive history of *C. diff* in the 2012-March 2017 period for inpatients and outpatients while all other time periods have lower-than-expected proportions ($p = .000$). In the follow-up period (**Table 37**), the 2002-2006 and 2012-March 2017 periods had higher than expected numbers of positive *C. diff* test results among inpatients while the 2007-2011 period had higher-than expected numbers of positive *C. diff* test results among outpatients ($p = .000$).

Table 36. Butler Memorial Hospital Nursing Home Patient Encounters over Four Time Periods by Patient Type (In and Outpatient) and Prior History of *Clostridium difficile* between 1985 and 1997 (Butler County Residents Only) (N = 14,158)

		History of C. diff		No History of C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	31	5.7	515	94.3	546	100.0	76.8	10.0
	2002-2006	147	10.0	1,318	90.0	1,465	100.0	77.6	10.4
	2007-2011	145	9.8	1,330	90.2	1,475	100.0	78.5	10.9
	2012- March 2017*	128	15.3	710	84.7	838	100.0	78.9	10.5
	Total	**451**	**10.4**	**3,873**	**89.6**	**4,324**	**100.0**	**78.1**	**10.6**
Outpatient									
	1997-2001	119	15.0	672	85.0	791	100.0	78.1	11.0
	2002-2006	611	17.9	2,806	82.1	3,417	100.0	80.5	10.4
	2007-2011	584	17.4	2,767	82.6	3,351	100.0	81.5	10.1
	2012-March 2017*	467	20.5	1,808	79.5	2,275	100.0	81.5	10.5
	Total	**1,781**	**18.1**	**8,053**	**81.9**	**9,834**	**100.0**	**80.9**	**10.4**
Total		**2,232**	**15.8**	**11,926**	**84.2**	**14,158**	**100.0**	**80.0**	**10.5**

Inpatient $\chi^{(3)} = 35.064$, p = .000, *Outpatient* $\chi^{(3)} = 15.150$, p = .002, *Total* $\chi^{(3)} = 48.877$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

Table 37. Butler Memorial Hospital Nursing Home Patient Encounters over Four Time Periods by Patient Type (In and Outpatient) and *Clostridium difficile* Test Result during Follow-up Period (1997-March 2017) (Butler County Residents Only) (N = 11,038)

		C. diff		No C. diff		Total			
		N	%	N	%	N	%	$\bar{x}$ age	SD
Inpatient									
	1997-2001	29	12.1	211	87.9	240	100.0	76.6	10.0
	2002-2006	125	15.4	689	84.6	814	100.0	76.9	10.8
	2007-2011	124	12.3	883	87.7	1,007	100.0	78.2	11.0
	2012-March 2017	113	19.4	468	80.6	581	100.0	78.5	10.6
	Total	**391**	**14.8**	**2,251**	**85.2**	**2,642**	**100.0**	**77.7**	**10.8**
Outpatient									
	1997-2001	125	20.2	494	79.8	619	100.0	79.0	11.4
	2002-2006	629	22.2	2,199	77.8	2,828	100.0	81.0	10.7
	2007-2011	608	20.6	2,339	79.4	2,947	100.0	81.8	9.9
	2012-March 2017	507	25.3	1,495	74.7	2,002	100.0	81.9	10.4
	Total	**1,869**	**22.2**	**6,527**	**77.7**	**8,396**	**100.0**	**81.3**	**10.5**
Total		**2,260**	**20.5**	**8,778**	**79.5**	**11,038**	**100.0**	**80.5**	**10.6**

Inpatient $\chi^{(3)} = 16.501$, p = .001, *Outpatient* $\chi^{(3)} = 16.911$, p = .001, *Total* $\chi^{(3)} = 32.634$, p = .000
*Testing method changed from enzyme immunoassay to molecular method at the end of 2011

4.5 MAPPING CLOSTRIDIUM DIFFICILE TEST RESULTS

Figures 12 through **19** are quantile maps of Butler County, Pennsylvania displaying rates of positive *C. diff* test results based on 2010 Census data by zip code over the four time periods (1997-2001, 2002-2006, 2007-2011, and 2012-March 2017). The maps show the change in rate of positive *C. diff* test results over time by the two age groups (18-64 and 65+). **Figures 12** through **15** show the rate of *C. diff* cases per 100,000 population in quantiles for Butler County Residents age 18-64. From the first period, 1997-2001, to the last, 2012-March 2017, the overall rate increases as evidenced by growing number of maroon quantiles. In **Figure 12** (1997-2001), the rate ranges from zero to 339.8 *C. diff* cases per 100,000 population. The rates in **Figure 13** (2002-

2006) range from zero to 647.7 *C. diff* cases per 100,000 population. Next, in the 2007-2011 period (**Figure 14**), *C. diff* rates range from zero to 684.9 per 100,000 population. Finally, in **Figure 15**, rates range from 0 to 2,727.3 per 100,000 population. These maps visually illustrate the increasing rates of *C. diff* shown in **Figures 4** through **11** as well as the fact that some zip codes increase over time while some decrease, or fluctuate, over time as the overall rate increases in this age group. In October 2011, Butler Memorial Hospital changed its *C. diff* testing method from enzyme immunoassay to a molecular method, which may contribute to some of the increase in prevalence rate between the 2007-2011 and 2012-March 2017 period.

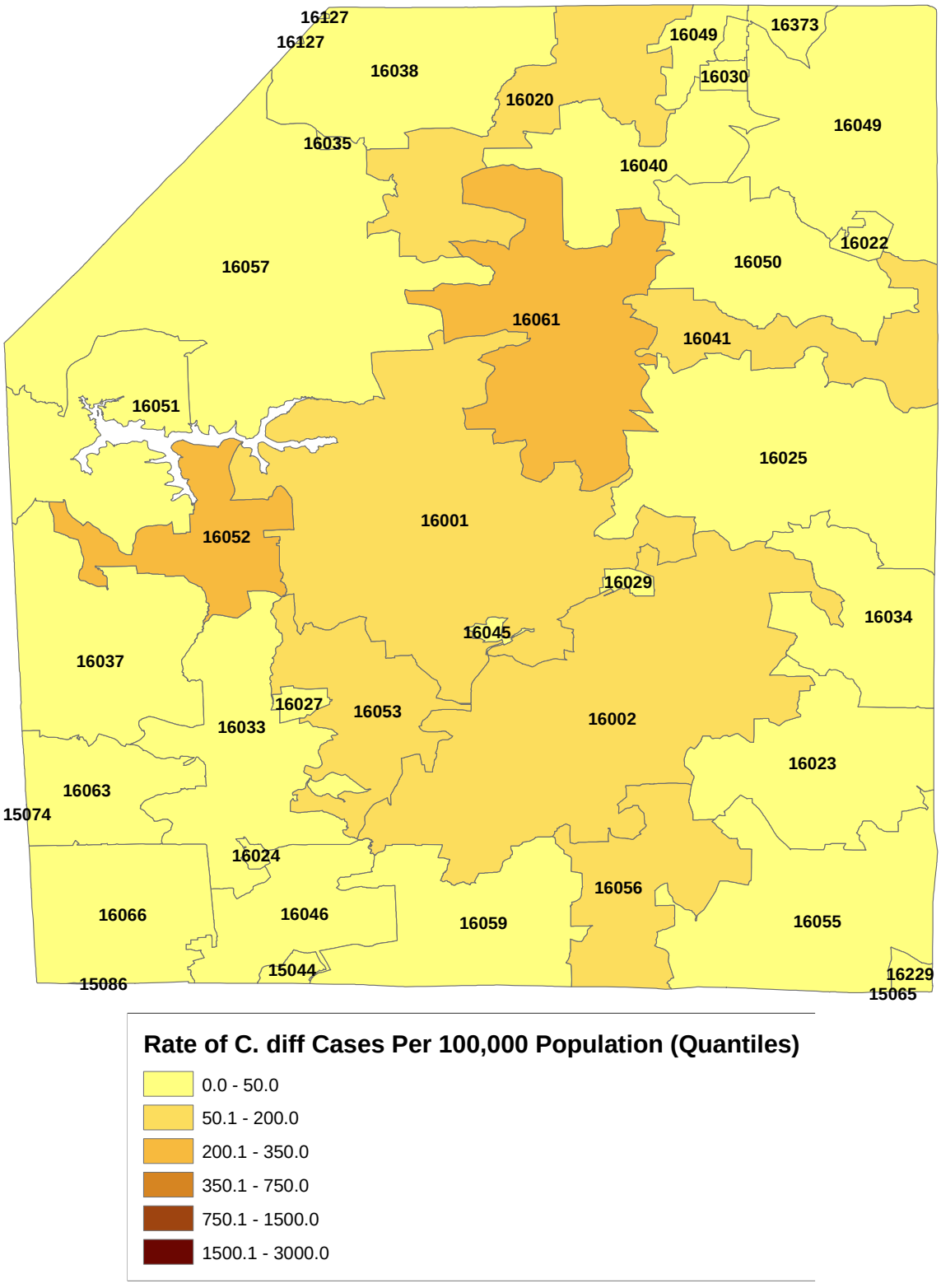


Figure 12. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 18-64 (1997-2001) per 100,000 Population based on 2010 Census Data

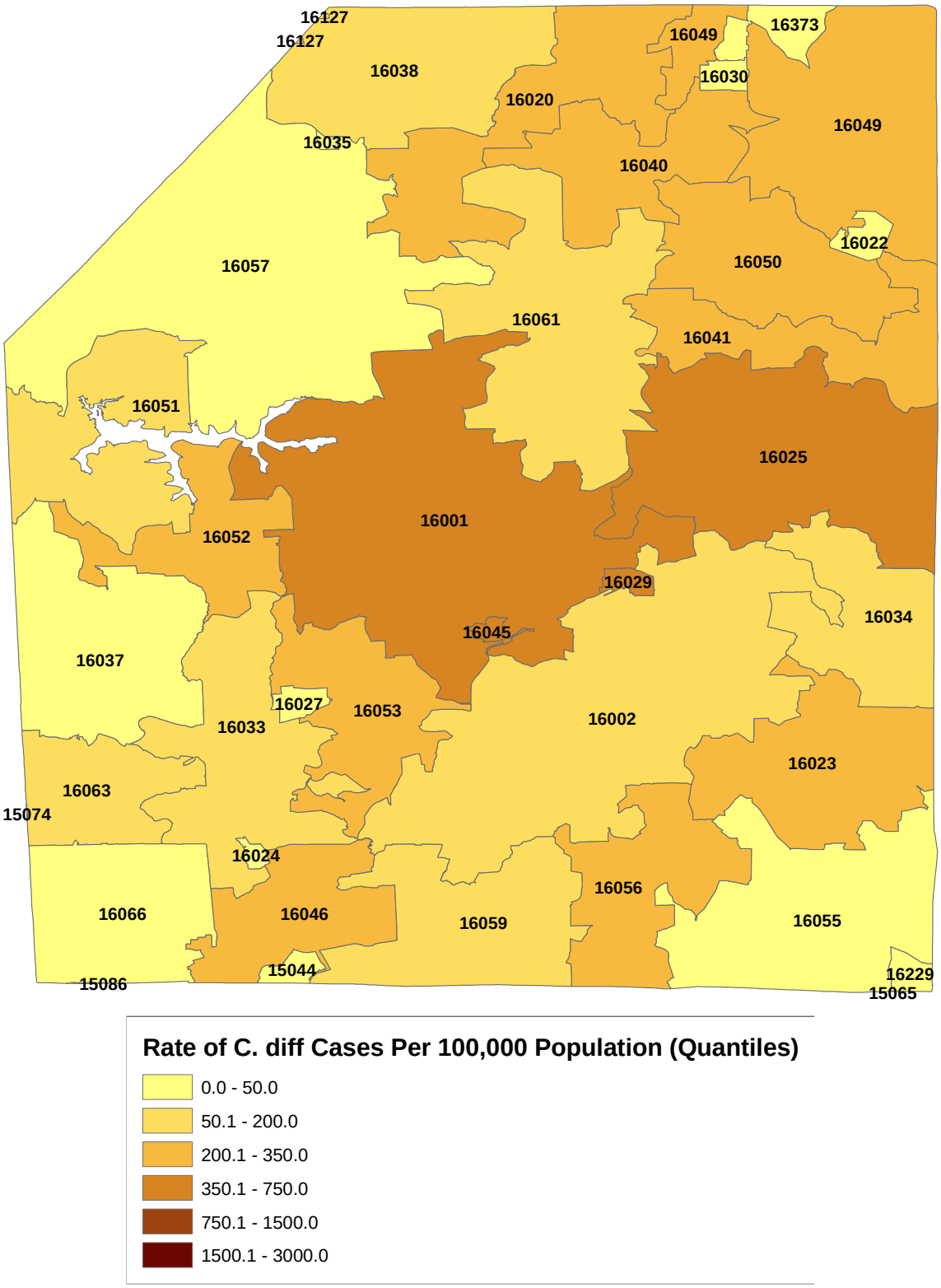


Figure 13. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 18-64 (2002-2006) per 100,000 Population based on 2010 Census Data

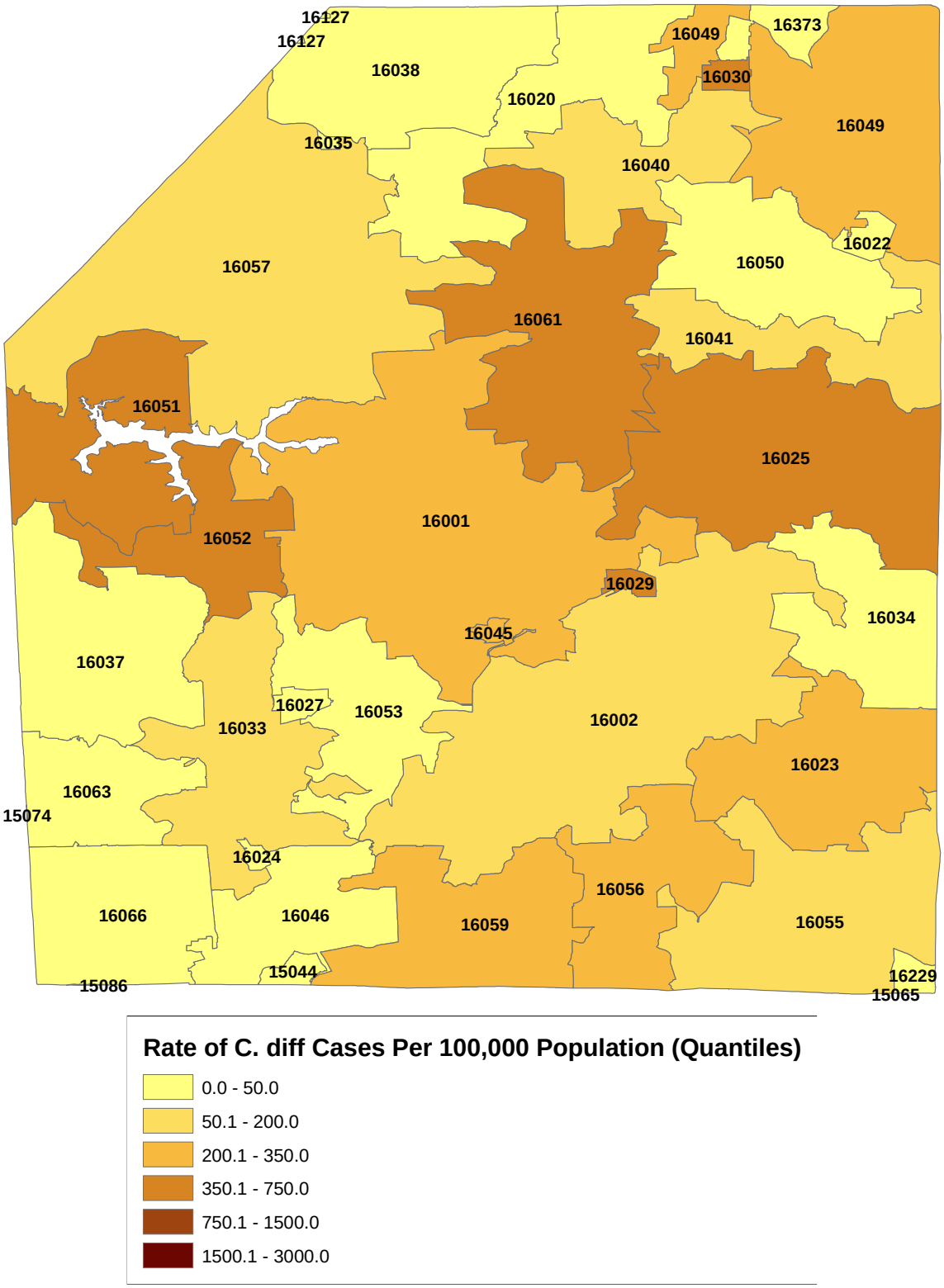


Figure 14. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 18-64 (2007-2011) per 100,000 Population based on 2010 Census Data

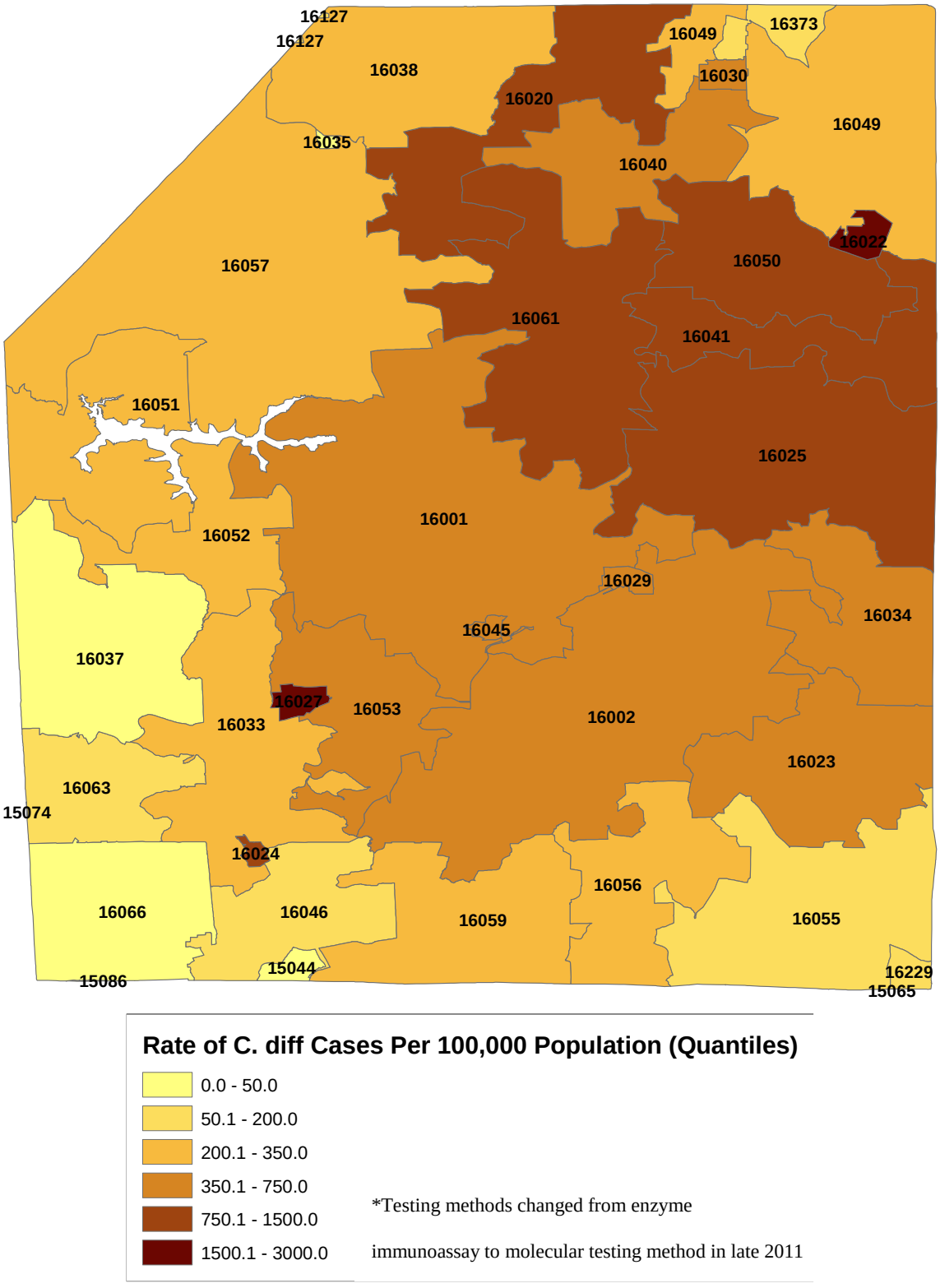


Figure 15. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 18-64 (2012- March 2017) per 100,000 Population based on 2010 Census Data

Figures 16 through **19** show the rate of *C. diff* cases per 10,000 population in quantiles for Butler County Residents age 65+. These maps show rates per 10,000 rather than per 100,000 since rates of positive *C. diff* test results are higher in this age range. From the first period, 1997-2001, to the last, 2012-March 2017, the overall rate increases as evidenced by growing number of dark orange and maroon quantiles. In **Figure 16** (1997-2001), the rate ranges from zero to 412.8 *C. diff* cases per 10,000 population. The rates in **Figure 17** (2002-2006) range from zero to 905.5 *C. diff* cases per 10,000 population. Next, in the 2007-2011 period (**Figure 18**), *C. diff* rates range from zero to 447.0 per 10,000 population, a slight decrease overall from the previous period. Finally, in **Figure 19**, the rate ranges from 0 to 1,262.1 per 10,000 population. These maps visually illustrate the increasing rates of *C. diff* shown in **Figures 4** through **11** as well as the fact that some zip codes increase over time while some decrease, or fluctuate, over time as the overall rate increases in this age group. Overall, in both age groups, these maps remove all nursing home patients to accurately display the change in trends among the non-nursing home population. In October 2011, Butler Memorial Hospital changed its *C. diff* testing method from enzyme immunoassay to a molecular method, which may contribute to some of the increase in prevalence rate between the 2007-2011 and 2012-March 2017 period.

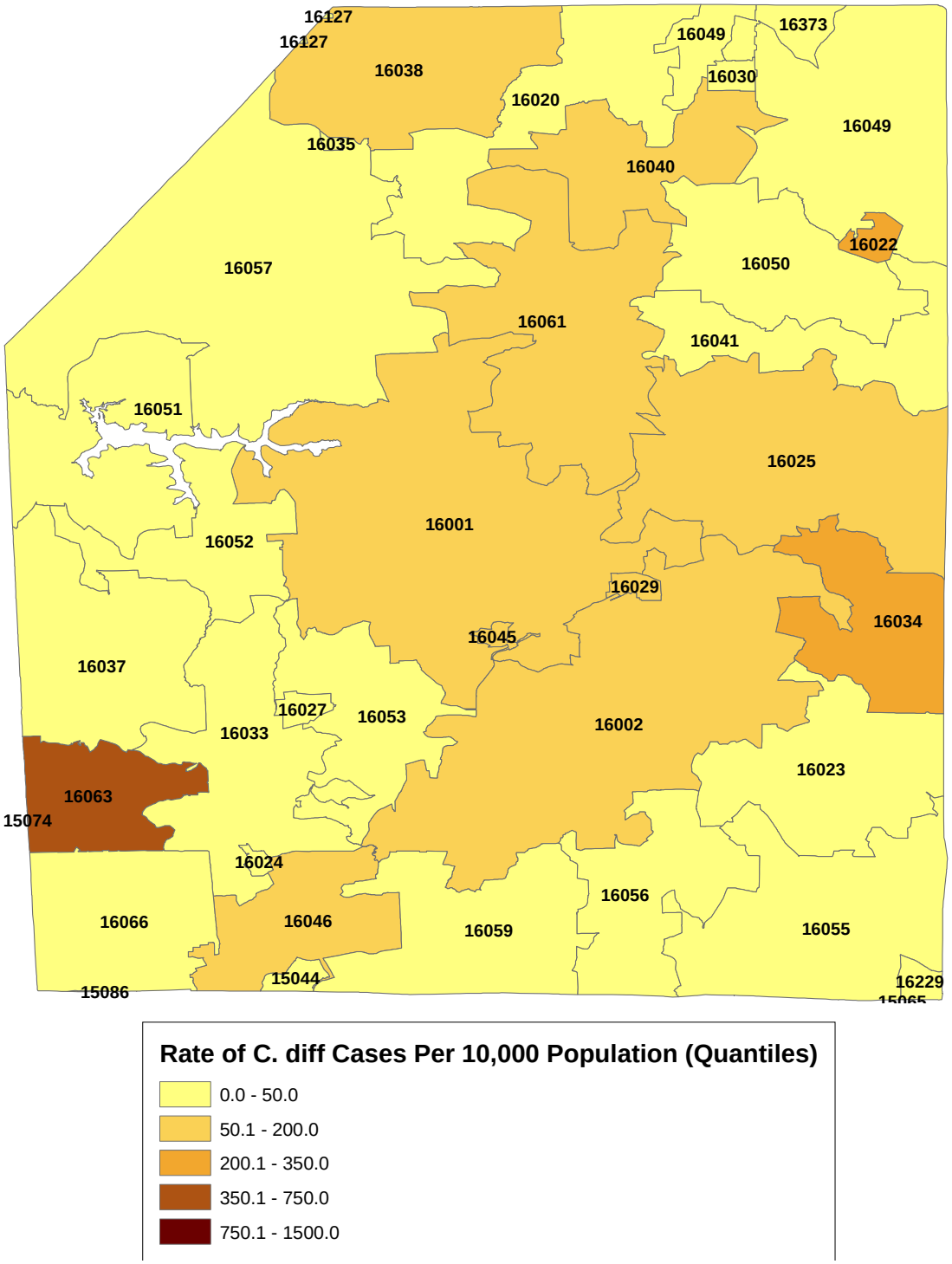


Figure 16. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 65+ (1997-2001) per 10,000 Population based on 2010 Census Data

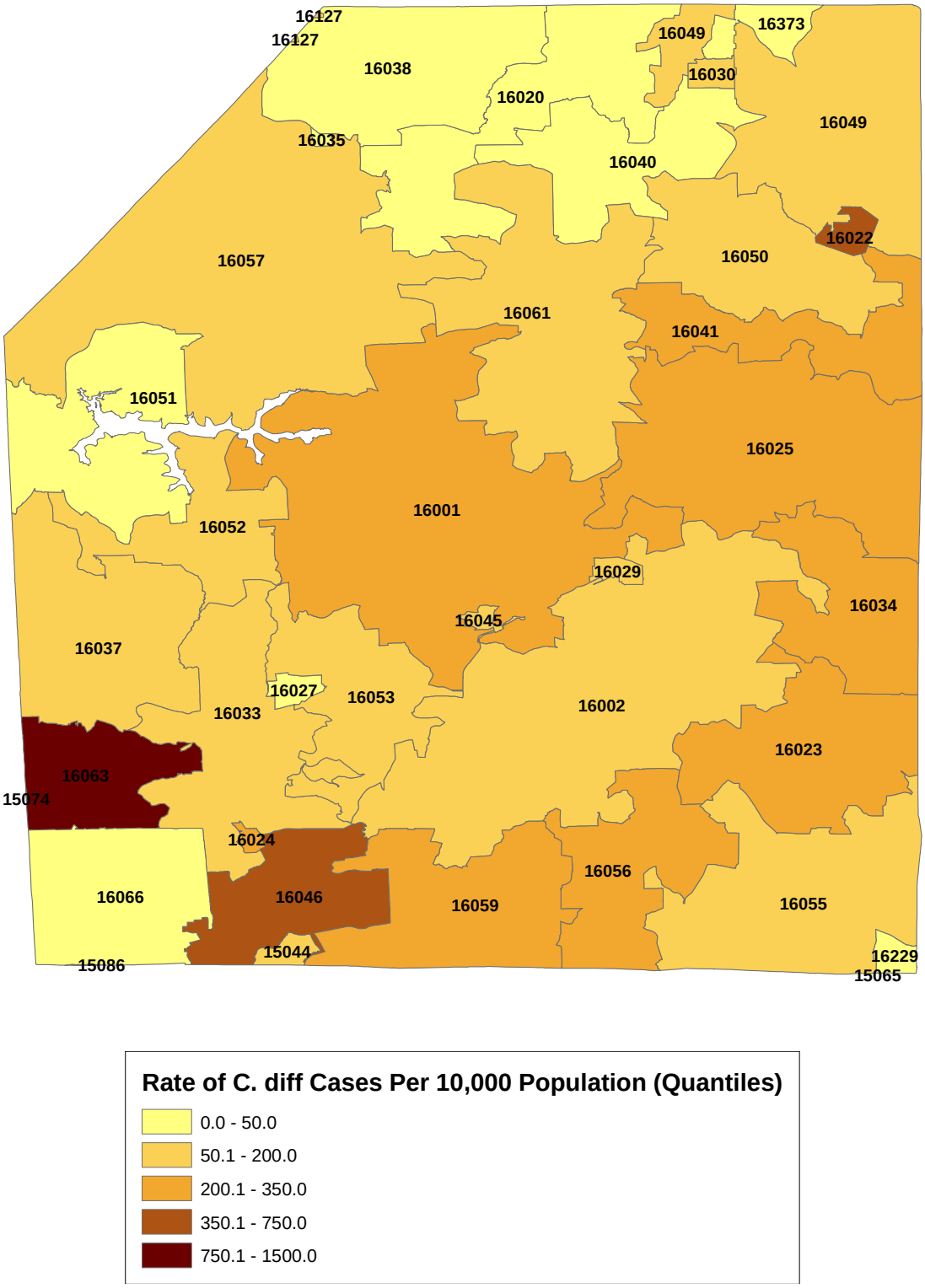


Figure 17. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 65+ (2002-2006) per 10,000 Population based on 2010 Census Data

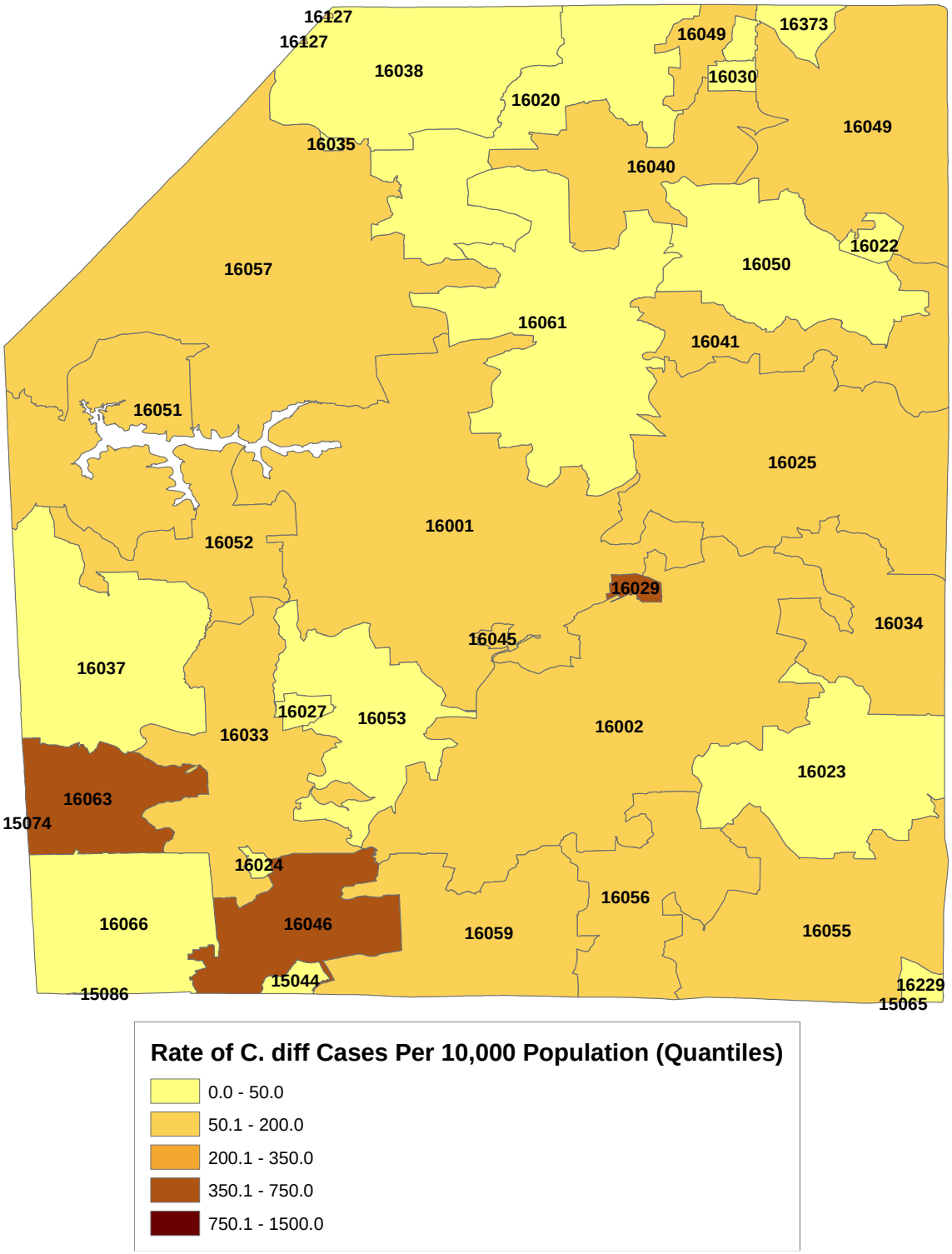


Figure 18. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 65+ (2007-2011) per 10,000 Population based on 2010 Census Data

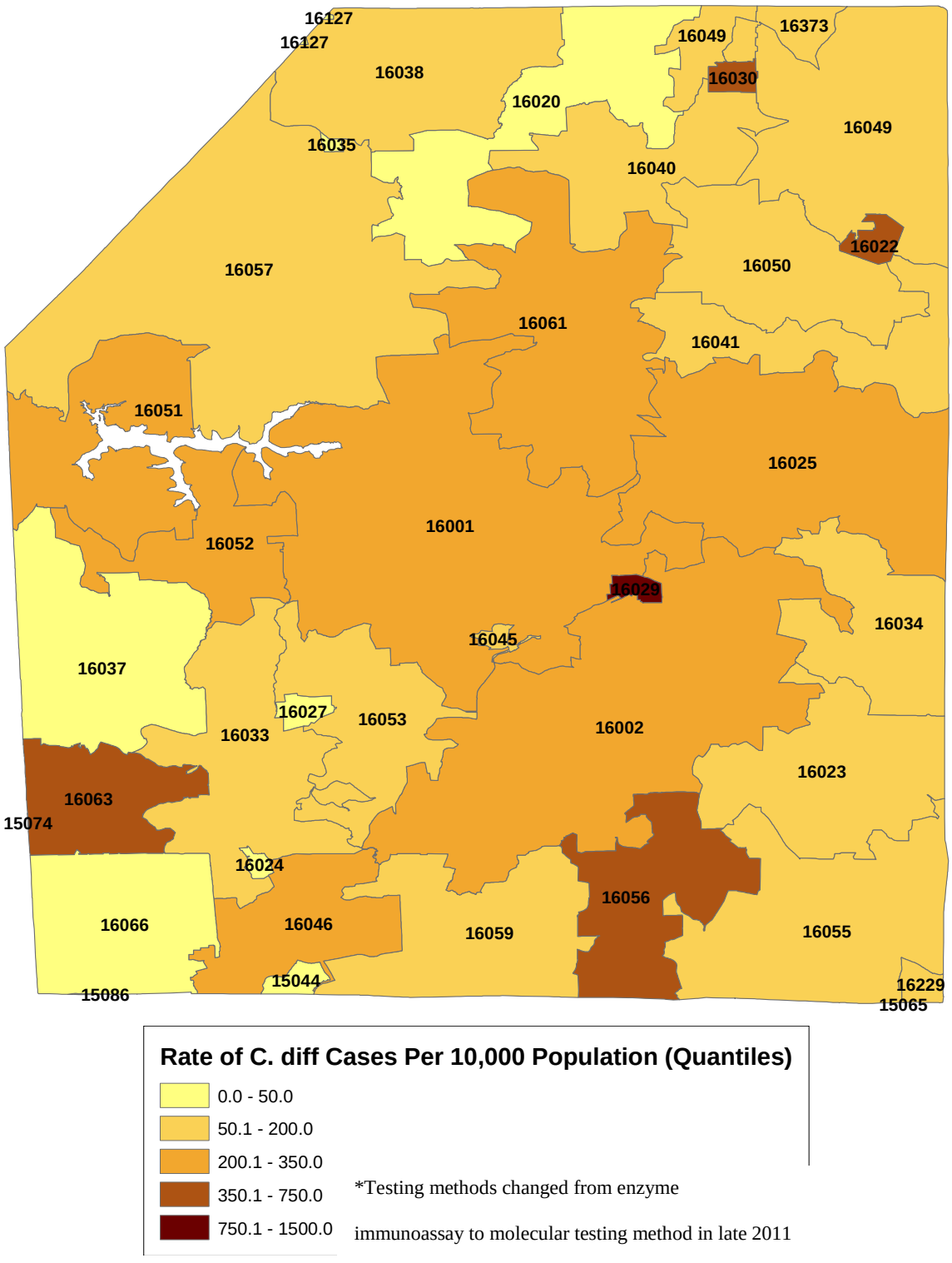


Figure 19. Prevalence Rates of Positive *Clostridium difficile* Test Results in Butler County among Non-Nursing Home Residents Aged 65+ (2012-March 2017) per 10,000 Population based on 2010 Census Data

4.6 ESTIMATING RISK OF SUBSEQUENT CLOSTRIDIUM DIFFICILE INFECTION BASED ON PRIOR HISTORY

To estimate the risk of subsequent *C. diff* infection based on prior history of *C. diff*, patients were queried based on individuals, or primary encounter; in other words, the first time they were a patient at Butler Memorial Hospital (either as inpatient or outpatient). Narrowing down to the individual level rather than remaining at the patient encounter level gives a better estimate of individual risk as using encounter data may inappropriately weight the relative risk. In addition, only patients who were tested for *C. diff* in the follow-up period were selected to calculate an accurate relative risk (RR); all patients had a test result for the variable History of *C. diff* as this was the basis for querying the dataset.

Table 38. Butler Memorial Hospital Primary Patient Encounters (In and Outpatient) Age 18-64 by History of *Clostridium difficile* (1985-1997) and subsequent *Clostridium difficile* testing (1997-March 2017) (N = 5,812)

	C. diff	**No *C. diff***	**Total**
	N, %	*N, %*	
History of *C. diff*	336 (42.9%)	448 (57.1%)	**784**
No History of *C.diff*	307 (6.1%)	4,721 (93.9%)	**5,028**
Total	**643**	**5,169**	**5,812**
RR = 7			

Among the 5,812 initial encounters (in and outpatients) 18-64 there were 784 individuals with a positive *C. diff* history (**Figure 38**). Of these, 42.9% (336) resulted in a subsequent positive *C. diff* test. Alternatively, among 5,028 initial encounters with a negative *C. diff* history, only 6.1% (307) resulted in a subsequent positive *C. diff* test while 93.9% (4,721) resulted in a negative test. Upon calculating the RR (the probability of a positive *C. diff* test occurring in those with a positive history of *C. diff* versus the probability of a positive *C. diff* test occurring in those with a negative

history of *C. diff*) it was found that among Butler Memorial Hospital primary patient encounters aged 18-64, those with a history of *C. diff* are seven times more likely to have a subsequent positive test than those with no history of *C. diff*.

Table 39. Butler Memorial Hospital Primary Patient Encounters (In and Outpatient) Age 65+ by History of *Clostridium difficile* (1985-1997) and subsequent *Clostridium difficile* testing (1997-March 2017)

	C. Diff	**No *C. diff***	**Total**
	N, %	*N, %*	
History of *C. diff*	1,277 (75.8%)	408 (24.2%)	**1,685**
No History of *C. diff*	587 (9.5%)	5,608 (90.5%)	**6,195**
Total	**1,864**	**6,016**	**7,880**
RR = 8			

Among the 7,880 initial encounters (in and outpatients) 65+ there were 1,685 individuals with a positive *C. diff* history (**Table 39**). Of these, 75.8% (1,277) resulted in a subsequent positive *C. diff* test. Alternatively, among 6,195 initial encounters with a negative *C. diff* history, 9.5% (587) resulted in a subsequent positive *C. diff* test while 90.5% (5,608) resulted in a negative test. Upon calculating the RR, it was found that among Butler Memorial Hospital primary patient encounters aged 65+, those with a history of *C. diff* are 8 times more likely to have a subsequent positive test than those with no history of *C. diff*. The RR in the 65+ age group (RR = 8) is slightly higher than that among the 18-64 age group (RR = 7). If the age groups had been broken down to the groups used in **Figures 2** and **3** (under 30, 31-44, 45-54, 55-64, 65-79, and 80+), there would have a gradual increase in RR would have been noted.

Table 40. Butler Memorial Hospital Nursing Home Primary Patient Encounters (In and Outpatient) by History of *Clostridium difficile* (1985-1997) and subsequent *Clostridium difficile* testing (1997-March 2017)

	C. Diff	**No *C. diff***	**Total**
	N, %	*N, %*	
History of *C. diff*	697 (83.7%)	136 (16.3%)	**833**
No History of *C. diff*	239 (9.9%)	2,121 (90.1%)	**2,410**
Total	**936**	**2,307**	**3,243**
RR = 8.3			

Among the 3,243 initial nursing home encounters (in and outpatients) there were 833 individuals with a positive *C. diff* history (**Table 40**). Of these, 83.7% (697) resulted in a subsequent positive *C. diff* test and 16.3% (136) resulted in a subsequent negative *C. diff* test. Alternatively, among 2,410 initial encounters with a negative *C. diff* history, 9.9% (239) resulted in a subsequent positive *C. diff* test while 90.1% (2,121) resulted in a negative test. Upon calculating the RR, it was found that among nursing home residents, those with a history of *C. diff* are 8.3 times more likely to have a subsequent positive test versus those with no history, which is similar to the RR in the 65+ age group. This similarity may be because many of these nursing home patients are in the 65+ age group shown previously. Also, since this dataset spans 30+ years, these nursing home residents may not have resided in a nursing home when they were previously tested for *C. diff*, which may explain why the percentage with a positive *C. diff* test and no previous history is slightly higher among nursing home residents. It is important to note, however, the increase in the percentage with a positive *C. diff* history and a positive test over the two age groups and among nursing home residents. In the 18-64 age group, 42.9% had a positive *C. diff* history and a positive subsequent test; in the 65+ age group, 75.8% had a positive *C. diff* history and a positive subsequent test; and in the nursing home group, 83.7% had a positive *C. diff* history and a positive subsequent test. This, combined with the increasing relative risk suggests that the risk

for testing positive for *C. diff* if you have tested positive in the past increases with age and residing in a nursing home.

4.7 PREDICTING A POSITIVE CLOSTIDIUM DIFFICILE TEST

To predict a positive *C. diff* test result for Butler County Residents over age 18 who were previously tested for *C. diff*, patient encounters with a *C. diff* test in the 1997-March 2017 follow up period were selected. **Table 41** shows the summary of the logistic regression analysis where *C. diff* test result (yes versus no) is the dependent variable. Independent variables included age, gender, history of *C. diff* (yes versus no), and nursing home resident status (yes versus no).

Table 41. Summary of Logistic Regression Analysis for Variables Predicting a Positive *C. diff* Test Result for Butler County Residents Over Age 18 Previously Tested for *C. diff* (N = 34,789)

	β	S.E.	Wald	df	Sig.	Exp(β)
Age	.019	.001	248.038	1	.000	1.019
Gender	.102	.038	7.223	1	.007	1.107
Yes or No History of *C. diff*	3.083	.037	7011.689	1	.000	21.821
Nursing Home Resident	.332	.041	66.953	1	.000	1.394
Constant	-4.244	.091	2182.781	1	.000	.014

In the model, age, gender, history of *C. diff*, and nursing home resident status were all significant predictors of a subsequent positive *C. diff* test. First, increasing age, as previously shown, increases the likelihood of a positive *C. diff* test result. Next, looking at gender, being a male (coded as 1) increases risk for *C. diff* versus being female (coded as 0) independent of all other variables in the model. **Table 41** shows that a positive history of *C. diff* (coded as 1) is the biggest predictor of a subsequent positive test. Finally, independent of age, gender, and prior

history, coming from a nursing home is a significant predictor of testing positive for *C. diff*, as previously hypothesized.

Tables 42, **43**, **44**, and **45** show the summary of the logistic regression analysis where *C. diff* test result (yes versus no) is the dependent variable. Independent variables included gender, history of *C. diff* (yes versus no), and nursing home resident status (yes versus no). **Table 42** considers Butler County residents age 18-34 only who were previously tested for *C. diff* and had a subsequent *C. diff* test in the 1997-March 2017 follow up period. Compared to **Table 41** that included all Butler County residents over age 18, gender and nursing home resident status is not a significant predictor of a subsequent positive *C. diff* test for encounters age 18-34; however, history of *C. diff* is still a significant predictor

Table 42. Summary of Logistic Regression Analysis for Variables Predicting a Positive *C. diff* Test Result for Butler County Residents Age 18-34 Previously Tested for *C. diff* (N = 2,178)

	β	S.E.	Wald	df	Sig.	Exp(β)
Gender	-.024	.190	.015	1	.901	.977
Yes or No History of *C. diff*	2.413	.183	173.214	1	.000	11.164
Nursing Home Resident	1.183	.616	3.686	1	.055	3.266
Constant	-3.250	.138	555.196	1	.000	.039

Table 43 considers Butler County residents age 35-49 only who were previously tested for *C. diff* and had a subsequent *C. diff* test in the 1997-March 2017 follow up period. In this model, gender is not a significant predictor of testing positive for *C. diff* while history of *C. diff* and being a nursing home resident is a significant predictor of *C. diff* for those aged 35-49.

Table 43. Summary of Logistic Regression Analysis for Variables Predicting a Positive *C. diff* Test Result for Butler County Residents Age 35-49 Previously Tested for *C. diff* (N = 3,441)

	β	S.E.	Wald	df	Sig.	Exp(β)
Gender	-.052	.139	.140	1	.708	.949
Yes or No History of *C. diff*	2.319	.138	280.888	1	.000	10.162
Nursing Home Resident	1.270	.216	34.539	1	.000	3.562
Constant	-3.134	.106	868.394	1	.000	.044

Table 44 considers Butler County residents age 50-64 only who were previously tested for *C. diff* and had a subsequent *C. diff* test in the 1997-March 2017 follow up period. In this model, gender is not a significant predictor of testing positive for *C. diff* while history of *C. diff* and being a nursing home resident is a significant predictor of *C. diff* for those aged 50-64.

Table 44. Summary of Logistic Regression Analysis for Variables Predicting a Positive *C. diff* Test Result for Butler County Residents Age 50-64 Previously Tested for *C. diff* (N = 6,056)

	β	S.E.	Wald	df	Sig.	Exp(β)
Gender	-.038	.090	.178	1	.673	.963
Yes or No History of *C. diff*	2.361	.089	706.317	1	.000	10.606
Nursing Home Resident	.658	.119	30.741	1	.000	1.930
Constant	-2.805	.071	1,560.252	1	.000	.061

Table 45 considers Butler County residents over age 65 only who were previously tested for *C. diff* and had a subsequent *C. diff* test in the 1997-March 2017 follow up period. In this model, gender, history of *C. diff*, and being a resident of a nursing home are all significant predictors of testing positive for *C. diff*. In all models for all age groups; however, having a prior history of *C. diff* is a significant predictor a subsequently positive test.

Table 45. Summary of Logistic Regression Analysis for Variables Predicting a Positive *C. diff* Test Result for Butler County Residents Over Age 65 Previously Tested for *C. diff* (N = 23,204)

	β	S.E.	Wald	Df	Sig.	Exp(β)
Gender	.103	.046	5.145	1	.023	1.109
Yes or No History of *C. diff*	3.357	.044	5,810.710	1	.000	28.706
Nursing Home Resident	.357	.044	66.186	1	.000	1.428
Constant	-2.831	.041	4,880.978	1	.000	.059

5.0 DISCUSSION

The purpose of this essay was to present the descriptive epidemiology of *C. diff* in Butler County Pennsylvania; show trends in *C. diff* over time in Butler County compared to national trends; utilize GIS to map the change in prevalence rates of *C. diff* over time; and to estimate the subsequent risk of testing positive for *C. diff* based on a previous test results.

As the epidemiology of *C. diff* changes and incidence increases, analyzing the trends in prevalence and the changing risk factors is of growing public health significance.[6,7] In addition, *C. diff* directly impacts and results from sanitation procedures in healthcare facilities and contributes to antibiotic resistance.[7,10] As the population in the United States ages, the incidence of infectious diseases that are more common with advancing age increases, resulting in greater challenges for public health.[8] The population of Butler County is also aging; the mean age of patients seen in Butler Memorial Hospital who have been tested for *C. diff* is 69.6 (**Table 1**). In addition, 25% of patient encounters over the last 30 years are nursing home residents (**Table 2**), indicating a population at elevated risk for *C. diff* infection.

We believe this may be the first study to present a long-term perspective on the descriptive and analytical epidemiology of a population of individuals tested in an earlier time period for *C. diff* and then followed over time for subsequent *C. diff* infection in both an outpatient and inpatient setting. Butler County Residents were tested for *C. diff* between 1985 and 1997 and followed forward to 2017 showed a higher proportion of patient encounters among females compared to males as well as a higher proportion of outpatients with both a history of *C. diff* and a subsequent positive *C. diff* test among encounters over age 65 and among nursing home residents, which indicate that advanced age and residing in a nursing home is a risk factor for *C. diff*. Analysis

confirmed that the relative risk of a patient testing positive for *C. diff* is higher if there was a previous positive test – especially among those over 65 and nursing home residents. Logistic regression analysis also indicated that a prior history of *C. diff* as the strongest predictor of a subsequent positive test, controlling for age, gender, and nursing home status.

An analysis of trends over time in both patients aged 18-64 and those over 65 revealed that among patient encounters by both history of *C. diff* and subsequent *C. diff* test results there is an overall increasing trend in positive *C. diff* history and positive *C. diff* test results over the last 20 years, consistent with increasing incidence of community-acquired and healthcare acquired *C. diff* in the United States.[5,6,7] In 2011, the CDC estimated that he incidence of HA-CDI was 95.3/100,000 population.[9] While this study was unable to estimate incidence of *C. diff,* GIS maps of *C. diff* prevalence rates by Butler County zip code revealed a large range of rates between zero and 684.9 cases per 100,000 population between 2007 and 2011 among those aged 18-64 and rates between zero and 447.0/ 10,000 population among those over 65 in the same time period. Similar to nationwide data, this study showed that the increase in *C. diff* in Butler County is due to the aging of the population and due to the high number of high risk patients coming from nursing homes.[8] Recommendations for the future include strict observance of currently recommended infection control measures such gloves, gowns, proper hand hygiene, as well as antibiotic stewardship.[10] Following these recommendations will not only reduce the burden of *C. diff* but also its associated economic burden.[6,19,22]

This study has several strengths. First, the dataset was a subset of Butler Memorial Hospital's patient records; this data, which spanned 30 years, allowed for an estimate of the burden of *C. diff* on Butler County and Butler Memorial Hospital. Second, since Butler County has a relatively stable population, the 20-year rate estimates are fairly accurate.[23] There are also several

weaknesses including the inability to calculate true incidence; the lack of molecular information on the strain of *C. diff* for each patient; and the ability to only calculate an estimate of risk. Recommended next steps include: prospectively testing for and recording the strain of *C. diff* for each patient to compare to national trends with the goal of identifying prevalent strains in Butler County; determining the increase in mortality risk from subsequent *C. diff* infections; and finally, should attempt to determine whether cases are community-acquired versus hospital-acquired to estimate the burden of CA-CDI versus HA-CDI on this population as CA-CDI is increasing in the United States among populations without traditional CDI risk factors.[6,11,13]

APPENDIX: DATA AGREEMENT WITH BUTLER MEMORIAL HOSPITAL

Butler Health System Data Privacy and Security Committee

June 30. 2016

To: Benjamin Hampton

Re: Data set request regarding patients with *Clostridium difficile* testing.

Attached: data field listing

Dear Mr. Hampton,

The Data Privacy and Security Committee has approved your request has approved your request for de-identified data on this cohort of patients. Per Section 164.514(a) of the HIPAA Privacy Rule, patients greater than 89 years will be excluded for privacy to comply with the privacy rule.

This data will be provided via encrypted flash drive, updates will be provided via encrypted flash drive or Citrix File Share.

We look forward to the results of your analysis.

Sincerely,

A. Thomas McGill, MD

CIO, VP Quality and Safety

Butler Health System

BIBLIOGRAPHY

1. Finney, J.M.T. (1893). Gastro-enterostomy for cicatrizing ulcer of the pylorus. *Bulletin of the Johns Hopkins Hospital, 4*(53).
2. Cameron, J. L. (2009). John Miller Turpin Finney: The First President of the American College of Surgeons. *Journal of the American College of Surgeons,208*(3), 327-332. doi:10.1016/j.jamcollsurg.2008.11.005
3. Bartlett, J. G., Chang, T. W., Gurwith, M., Gorbach, S. L., & Onderdonk, A. B. (1978). Antibiotic-Associated Pseudomembranous Colitis Due to Toxin-Producing Clostridia. *New England Journal of Medicine,298*(10), 531-534. doi:10.1056/nejm197803092981003
4. Bartlett, J. G., Moon, N., Chang, T. W., Taylor, N., & Onderdonk, A. B. (1978). Role of Clostridium difficile in antibiotic -associated pseudomembranous colitis. *Gastroenterology,75*(5), 778-782.
5. Lessa, F. C., Gould, C. V., & Mcdonald, L. C. (2012). Current Status of Clostridium difficile Infection Epidemiology. *Clinical Infectious Diseases,55*(Suppl 2), S65-S70. doi:10.1093/cid/cis319
6. Depestel, D. D., & Aronoff, D. M. (2013). Epidemiology of Clostridium difficile Infection. *Journal of Pharmacy Practice,26*(5), 464-475. doi:10.1177/0897190013499521
7. Riddle, D. J., & Dubberke, E. R. (2009). Trends in *Clostridium difficile* Disease: Epidemiology and Intervention. *Infections in Medicine, 26*(7), 211–220.
8. Khanna, S., & Pardi, D. S. (2010). The growing incidence and severity of Clostridium difficile infection in inpatient and outpatient settings. *Expert Review of Gastroenterology & Hepatology*, *4*(4), 409+. Retrieved from http://go.galegroup.com.pitt.idm.oclc.org/ps/i.do?p=AONE&sw=w&u=upitt_main&v=2.1&it=r&id=GALE%7CA273044912&sid=summon&asid=a715445c3f3fd78bed570c9c965b9271\
9. Lessa, F. C., Mu, Y., Bamberg, W. M., Beldavs, Z. G., Dumyati, G. K., Dunn, J. R., . . . Mcdonald, L. C. (2015). Burden of Clostridium difficile Infection in the United States. *New England Journal of Medicine,372*(9), 825-834. doi:10.1056/nejmoa1408913
10. Cohen, S. H., Gerding, D. N., Johnson, S., Kelly, C. P., Loo, V. G., Mcdonald, L., . . . Wilcox, M. H. (2010). Clinical Practice Guidelines for Clostridium difficile Infection in Adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infection Control and Hospital Epidemiology,31*(5), 431-455. doi:10.1086/651706
11. Khanna, S., Pardi, D. S., Aronson, S. L., Kammer, P. P., Orenstein, R., Sauver, J. L., . . . Zinsmeister, A. R. (2011). The Epidemiology of Community-Acquired Clostridium difficile Infection: A Population-Based Study. *The American Journal of Gastroenterology,107*(1), 89-95. doi:10.1038/ajg.2011.398
12. Taori, S. K., Wroe, A., Hardie, A., Gibb, A. P., & Poxton, I. R. (2014). A Prospective Study of Community-associated Clostridium difficile Infections: The Role of Antibiotics and Co-infections. *Journal of Infection,69*(2), 134-144. doi:10.1016/j.jinf.2014.04.002

13. Kuntz, J. L., Chrischilles, E. A., Pendergast, J. F., Herwaldt, L. A., & Polgreen, P. M. (2011). Incidence of and risk factors for community-associated Clostridium difficile infection: A nested case-control study. *BMC Infectious Diseases,11*(1). doi:10.1186/1471-2334-11-194
14. Leekha, S., Aronhalt, K. C., Sloan, L. M., Patel, R., & Orenstein, R. (2013). Asymptomatic Clostridium difficile colonization in a tertiary care hospital: Admission prevalence and risk factors. *American Journal of Infection Control,41*(5), 390-393. doi:10.1016/j.ajic.2012.09.023
15. Kong, L. Y., Dendukuri, N., Schiller, I., Bourgault, A., Brassard, P., Poirier, L., . . . Loo, V. G. (2015). Predictors of asymptomatic Clostridium difficile colonization on hospital admission. *American Journal of Infection Control,43*(3), 248-253. doi:10.1016/j.ajic.2014.11.024
16. Evans, C. T., & Safdar, N. (2015). Current Trends in the Epidemiology and Outcomes of Clostridium difficile Infection. *Clinical Infectious Diseases,60*(Suppl 2), S66-S71. doi:10.1093/cid/civ140
17. Khanna, S., & Gupta, A. (2014). Community-acquired Clostridium difficile infection: an increasing public health threat. *Infection and Drug Resistance,* 63-72. doi:10.2147/idr.s46780
18. Jamal, W., Pauline, E., & Rotimi, V. (2015). A prospective study of community-associated Clostridium difficile infection in Kuwait: Epidemiology and ribotypes. *Anaerobe,35,* 28-32. doi:10.1016/j.anaerobe.2015.06.006
19. Collins, C. E., Ayturk, M. D., Flahive, J. M., Emhoff, T. A., Anderson, F. A., & Santry, H. P. (2014). Epidemiology and Outcomes of Community-Acquired Clostridium difficile Infections in Medicare Beneficiaries. *Journal of the American College of Surgeons,218*(6), 1141-1147. doi:10.1016/j.jamcollsurg.2014.01.053
20. Chitnis, A. S., Holzbauer, S. M., Belflower, R. M., Winston, L. G., Bamberg, W. M., Lyons, C., . . . Lessa, F. C. (2013). Epidemiology of Community-Associated Clostridium difficile Infection, 2009 Through 2011. *JAMA Internal Medicine,173*(14), 1359-1367. doi:10.1001/jamainternmed.2013.7056
21. Alasmari, F., Seiler, S. M., Hink, T., Burnham, C. D., & Dubberke, E. R. (2014). Prevalence and Risk Factors for Asymptomatic Clostridium difficile Carriage. *Clinical Infectious Diseases,59*(2), 216-222. doi:10.1093/cid/ciu258
22. McGlone, S. M., Bailey, R. R., Zimmer, S. M., Popovich, M. J., Tian, Y., Ufberg, P., . . . Lee, B. Y. (2011). The economic burden of Clostridium difficile. *Clinical Microbiology and Infection,18,* 282-289. doi:10.111/j.1469-0691.2011.03571.x
23. Briem, C. (2011). Migration Trends in the Pittsburgh Region: Update Through 2010. *Program in Urban and Regional Analysis University Center for Social and Urban Research*. Pittsburgh, PA: University of Pittsburgh.